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# *The American Heart Journal*

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# The American Heart Journal

VOL. V AUGUST, 1930 No. 6

## Original Communications

### BUNDLE-BRANCH BLOCK WITH SHORT P-R INTERVAL IN HEALTHY YOUNG PEOPLE PRONE TO PAROXYSMAL TACHYCARDIA

LOUIS WOLFF, M.D., BOSTON, MASS., JOHN PARKINSON, M.D., LONDON, ENG., AND PAUL D. WHITE, M.D., BOSTON, MASS.

ABERRANT ventricular complexes of the type generally recognized as indicating bundle-branch block were first produced by Eppinger and Rothberger,[3, 4] by the experimental division of the right branch of the His bundle. Eppinger and Stoerk[5] observed similar curves in five patients, and at autopsy demonstrated division of the right branch of the His bundle in two of these. The work of Cohn and Lewis,[2] and of Carter[1] indicated, however, that gross lesions of the main branches are not invariably found at autopsy in patients who during life present this type of electrocardiogram.

Following these original contributions to the subject, bundle-branch block curves have been observed as a temporary sign during infections, congestive failure, coronary thrombosis, tachycardias, and various toxic states. In most if not in all of the reported cases the abnormal curves occurred in patients with definite structural heart disease, or with extreme tachycardia. The references already cited[1, 2] indicate that the type of electrocardiogram under discussion may be obtained in the absence of gross division of a bundle branch.

Experimentally, bundle-branch block curves may be obtained in normal hearts by causing an impulse to enter one bundle branch later than the other. The same result would be produced should the impulse travel through the bundle branches at different speeds or by an aberrant course. That such a mechanism may occur in human beings with normal hearts seems likely from a study of the cases described in the present paper, the presumption being that vagal stimulation may, in certain individuals, give rise to aberrant ventricular complexes.

We have observed the occurrence of bundle-branch block curves in healthy young adults and children with apparently normal hearts. The curves may be typically those of complete right or left bundle-branch block, or of intermediate or lesser grades of aberration. Spon-

taneously, or following release of vagal tone by exercise or atropinization, there is a transition from aberrant ventricular complexes to perfectly normal ones. Coincident with the change to normal ventricular complexes, the P-R interval increases from an unusually short one (never greater than 0.1 second) to one of normal length, frequently almost doubling itself. In other words release of vagal tone is accompanied by a lengthening of the P-R interval; this paradoxical vagal effect is of considerable interest; its mechanism is obscure. Another feature observed in these patients is the occurrence of paroxysmal tachycardia, or paroxysmal fibrillation or perhaps flutter.

The phenomena just mentioned have been present more or less consistently in all of our patients. The combination constitutes a type of rhythm, or mechanism, which has not yet been described as such; it is probably not rare. Considerable importance attaches to the recognition that bundle-branch block curves do not always indicate organic heart disease. The ease with which such cases may be recognized will be apparent from the description of our cases.

## CASE REPORTS

*Case I.* S.O.S., married, male, aged 35 years when first seen by us April 2, 1928.

*Occupation.* Physical director.

*Chief complaint.* Palpitation off and on for the past ten years.

*Present history.* His general health has always been excellent. Attacks of palpitation, which began ten years ago, are brought on by excitement or exertion, and once followed the drinking of one or two glasses of whiskey. During the attacks, which come on about once a week and last about half an hour, he is conscious of the heart beating rapidly and irregularly, and occasionally during these attacks he has listened to his own heart with a stethoscope, finding a grossly irregular rhythm. This has been confirmed by his physician. During the paroxysm he feels somewhat weak but continues his activity. He does wrestling, boxing, swimming and road work, running ten miles without any undue symptoms. A paroxysm of fibrillation once came on while he was swimming and ended while the swimming was continued. Less frequent attacks of a different type of palpitation occur in which the heart beats much faster and is regular except for occasional intermittence. Blood seems to rush to the head at such times. The attack is stopped by bending forward so that his head is low. Many examinations in the past fifteen years have failed to reveal any evidence of heart disease, though occasionally the heart was said to be irregular.

Active service in the army lasted from May, 1917 to August, 1919. The patient is of a "nervous," introspective type.

*Past history.* Negative except for Neisserian infection seventeen years ago, mild influenza in 1918, and psoriasis one year ago.

*Marital history.* Married five years. Wife living and well, but has never been pregnant.

*Physical examination.* General condition excellent. Well developed and nourished, muscular, healthy athlete in the pink of condition. The entire examination was negative except that the tonsils were large and the tip of the spleen was just palpable. *Heart.* The cardiac impulse was felt in the fifth intercostal space 7.5 cm. to the left of the midsternal line. The left border of dulness was 8 cm. and the midclavicular line was 9.5 cm. to the left of the midsternal line. The heart

rate was irregular, varying between 50 and 80 per minute, but there was a dominant rhythm. After exercise the heart accelerated moderately, but was normal in rate again in one to two minutes. The sounds were of good quality; the first apical sound was reduplicated; there were no murmurs. The pulse form and artery walls were normal. There was no arcus senilis. Blood pressure was 104 mm. mercury systolic, and 70 diastolic.

*Roentgen ray report* ("7 foot plate"). The heart shadow was rather round and wide acrosss the auricles, but was not "mitral shaped." The transverse diameter was within normal limits. The supracardiac shadow was small. The aorta seemed narrowed in both antero-posterior and oblique views. The measurements were as

Fig. 1.—(Case I) Right bundle-branch block. The P-R interval is 0.1 second. The rate is 72. Time intervals for this and succeeding figures = 0.2 second. Horizontal lines cut off intervals of $10^{-4}$ volt.

follows: to the right of the midsternum 5.9 cm., to the left 8.2, total transverse diameter 14.1, length 14.5, base 13.5, width of great vessels 5.2, and internal diameter of thorax 30.5.

The blood Wassermann reaction was negative.

*Later notes.* (1) April 23, 1928. Is taking quinidine sulphate in daily rations of grs. ix. There have been no more paroxysms of fibrillation.

(2) June 15, 1928. In perfect health. No more paroxysms. Is not taking quinidine.

(3) August 24, 1928. Except for one or two very short paroxysms of auricular fibrillation he has been in excellent health.

(4) October 1929. He has been in excellent health, and has done strenuous athletic work. Several attacks of paroxysmal tachycardia have occurred, but none of auricular fibrillation. Physical examination negative.

*Electrocardiograms.* Numerous electrocardiograms were taken. When the patient was at rest the usual finding was normal rhythm at a rate of about seventy, with slight sinus arrhythmia, and intraventricular block of the "right bundle-branch type." The QRS complexes were greater than 0.1 second in duration, with the T-waves directed opposite to the chief deflection. The P-waves were poorly marked, and the P-R interval measured 0.10 second (Fig. 1). Exercise (running up and down four flights of stairs) produced a sino-auricular tachycardia rate 140-120, with

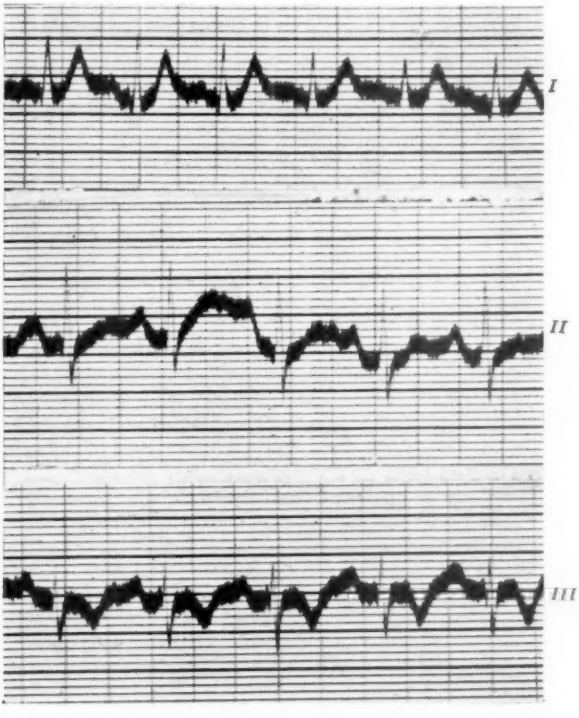


Fig. 2.—(Case I) Immediately after exercise (running up and down four flights of stairs). Sino-auricular tachycardia, rate 140 to 120. The ventricular complexes are normal, the P-waves are better marked, and the P-R interval is 0.16 second.

perfectly normal ventricular complexes throughout (Fig. 2). The P-waves were now better marked, and the P-R interval definitely longer (0.16 second). After a rest of twenty minutes the bundle-branch block complexes had returned. Following the injection of atropine sulphate (gr. 1/30 subcutaneously) the ventricular complexes again became normal, and the P-R interval measured 0.15 to 0.16 second (Fig. 3).

The last electrocardiogram, taken in October 1929, showed the normal type of complexes which changed to right bundle-branch block when pressure was exerted on the right vagus nerve.

(We are indebted to Dr. Hyman Morrison for the privilege of studying this case.)

*Case II.* D.C., single, male, aged 18½ years when first seen by us March 20, 1928.

*Occupation.* College freshman.

*Present history.* His general health had always been excellent. Four years ago he had his first attack of rapid vigorous heart action with sudden onset and offset, lasting fifteen minutes. The heart was regular at a rate of about 160. This had recurred from 3 to 4 times a year since, coming irregularly every few weeks to months. The attacks usually came when he was quiet, except once when he was struck in the chest in a soccer game. He lay down when an attack occurred and it quickly passed off, never lasting more than one-half hour. The last attack came three months ago while sitting at the edge of the swimming tank. A doctor who happened to be present stopped the attack by vagal pressure.

During the attacks of tachycardia there were slight dyspnea and an aching in the back of the neck. At other times there were no symptoms.

*Past history* and *family history* were irrelevant. He was not a blue baby.

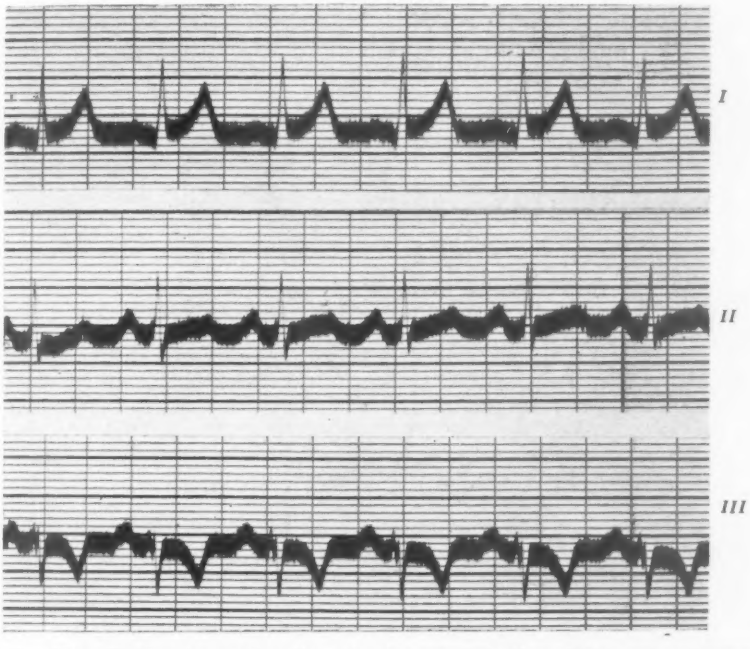


Fig. 3.—(Case I) One hour after the subcutaneous injection of 1/30 grain of atropine sulphate. The rate is 140, the ventricular complexes are normal, and the P-R interval is 0.15 to 0.16 second.

*Physical Examination*, which showed a large and robust athlete, apparently in excellent health, was entirely negative. The maximum apex impulse of the heart was felt behind the fifth rib, 8 cm. to the left of the midsternal line. The left border of dulness was 7.5 cm. from the midsternum and the midclavicular line was 9 cm. to the left of the midsternal line. The sounds were of good quality, the first apical sound double. At the apex a slight systolic murmur was audible when the patient was recumbent. The blood pressure was 115-120 mm. mercury systolic, and 60 diastolic. The heart rate was 68, and the response to exercise was good.

A *teleroentgenogram* ("7 foot plate") of the heart was normal.

*Basal metabolism* was normal.

*Electrocardiograms* showed aberrant ventricular complexes (intraventricular block) and an unusually short P-R interval (Fig. 4). After exercise the ventricular complexes assumed a normal physiological form and the P-R interval became distinctly longer (Fig. 5).

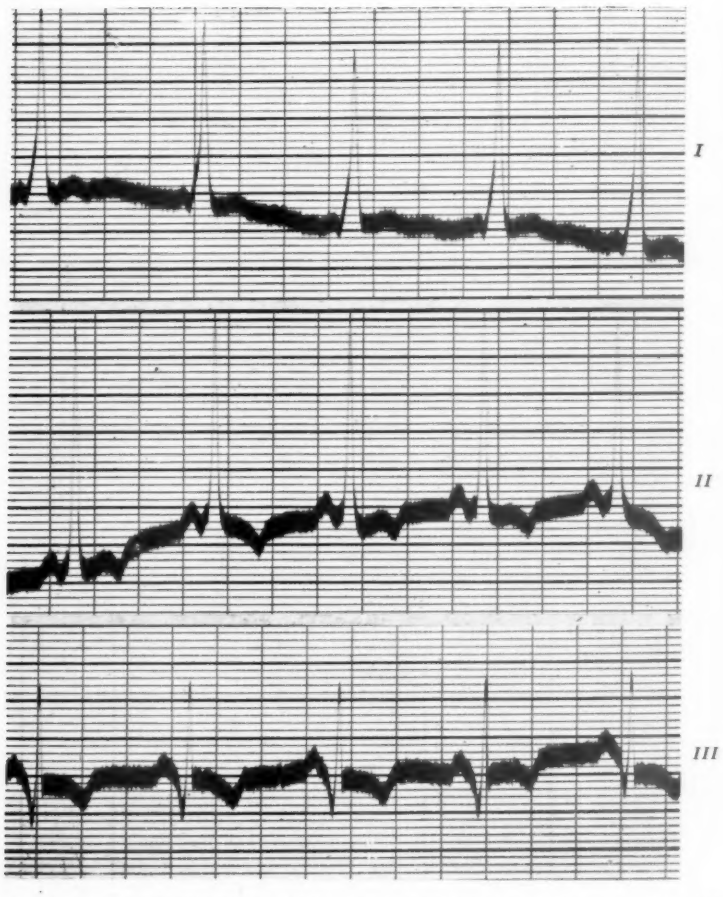


Fig. 4.—(Case II) Intraventricular block. The P-R interval is 0.1 second. Rate 96.

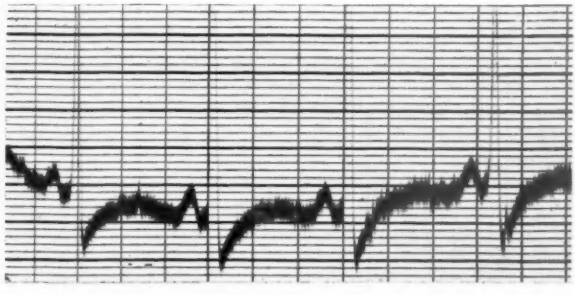

Fig. 5.—(Case II) Immediately after exercise. The ventricular complexes are normal except for deformity of the S wave and S-T interval by artefact (high resistance, resulting in over-shooting). The T-wave is upright. The P-R interval is 0.15 second Rate 96.

When last heard from in the fall of 1929 this young man was very well and active.

*Case III.* C.P.R., male, aged 21 years when first seen by us on June 29, 1927.

*History.* He complained of attacks of palpitation which had recurred ever since school days. The attacks had become more frequent so that he had one or two almost daily. They began suddenly without apparent cause, lasted from a few minutes to three hours, and stopped suddenly. Lying down or bending over usually stopped the attacks. He said that he had always been short-winded, but that he had been quite well except for the palpitation. There was no rheumatic history.

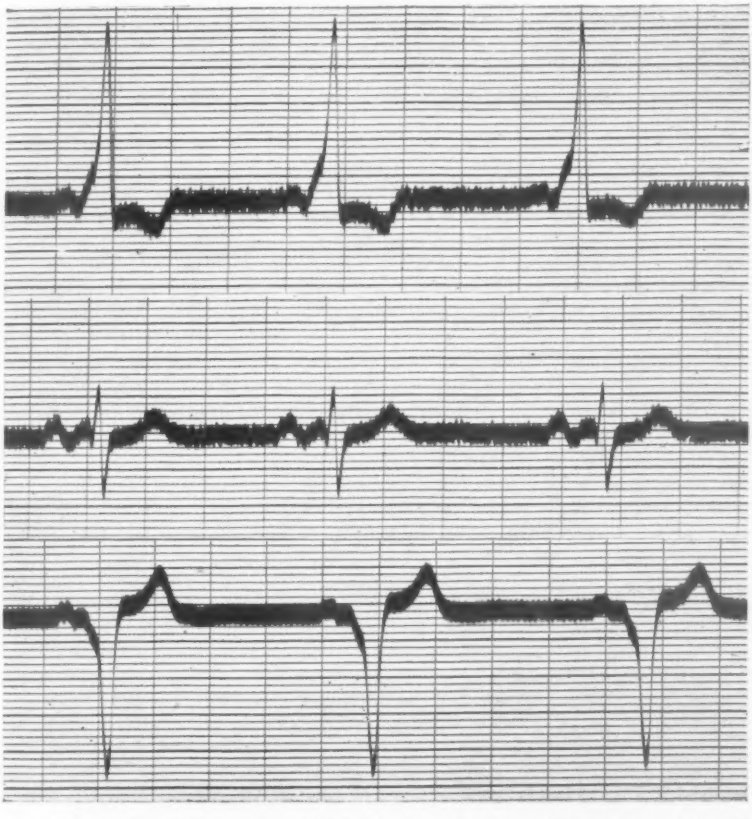


Fig. 6.—(Case III) Right bundle-branch block. The P-R interval is well under 0.1 second. The rate varies between 60 and 70.

*Examination* showed no abnormal signs and he looked plump and well. The blood pressure was 135 mm. mercury systolic and 80 mm. diastolic.

*Radioscopy* showed no enlargement.

A routine *electrocardiogram* showed right bundle-branch block, upright P-waves in all leads, and a P-R interval well under 0.1 second (Fig. 6).

On February 17, 1928 he was seen after a paroxysm of tachycardia lasting seven hours. Electrocardiograms now showed normal complexes (Fig. 7), with recurrent periods of the abnormal curve recorded in 1927. The P-waves were identical when the QRS waves were normal and when they were of the type designated as indicating bundle-branch block; the P-R interval, however, was well under 0.1 second

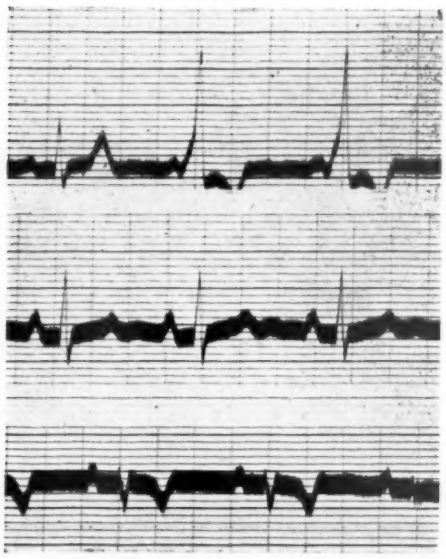


Fig. 7.—(Case III) After a paroxysm of tachycardia lasting seven hours. The ventricular complexes are normal, but occasionally there is reversion to the abnormal form. The P-R interval is almost 0.2 second. The P-waves are notched, and identical in Figs. 6 and 7.

Fig. 8.—(Case III) Two years after Fig. 6 was taken. Normal physiological curves.

when bundle-branch block curves were present, and almost 0.2 second when the QRS complexes were normal. (Fig. 7.)

On September 27, 1928, it was reported that his paroxysms were less frequent.

On the 30th of August, 1929, he was re-examined. There had been only one paroxysm of tachycardia during the previous twelve months. The electrocardiogram was now a normal physiological one (Fig. 8).

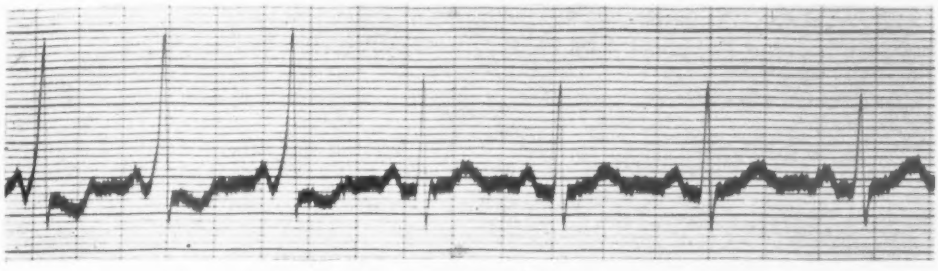

Fig. 9.—(Case IV) Spontaneous reversion from bundle-branch block curves to normal ones. The form of the P-wave remains unaltered, but the P-R interval changes from 0.09 second to 0.15 second.

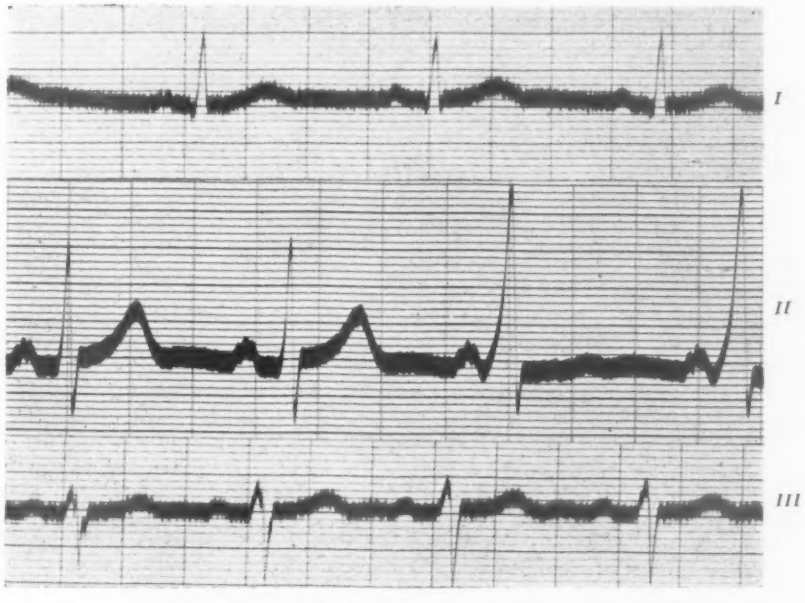


Fig. 10.—(Case IV) Normal physiological complexes. P-R interval 0.15 second. In Lead II there is a transition to the abnormal form and short P-R interval.

*Case IV.* C.A., male, aged 16 years when first seen by us on January 7, 1926. There was a history of occasional palpitation. The heart would suddenly become rapid, generally on exertion. The last bad attack was after playing football. There were no other symptoms, and no rheumatic history.

*Examination* revealed no abnormal signs. The heart rate was slightly rapid, with an irregularity which at first was thought to be a sinus arrhythmia. The blood pressure was 135 mm. mercury systolic, and 75 diastolic.

*Radioscopy* showed no enlargement.

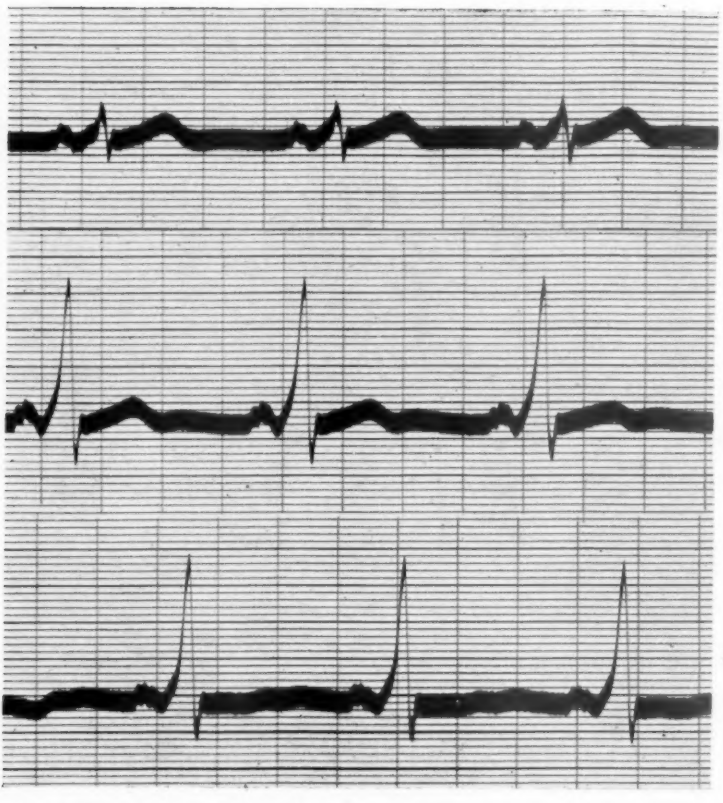


Fig. 11.—(Case IV) Bundle-branch block. The P-R interval is less than 0.1 second. The P-waves are identical in Figs. 10 and 11; note the peculiar notching of the P-waves.

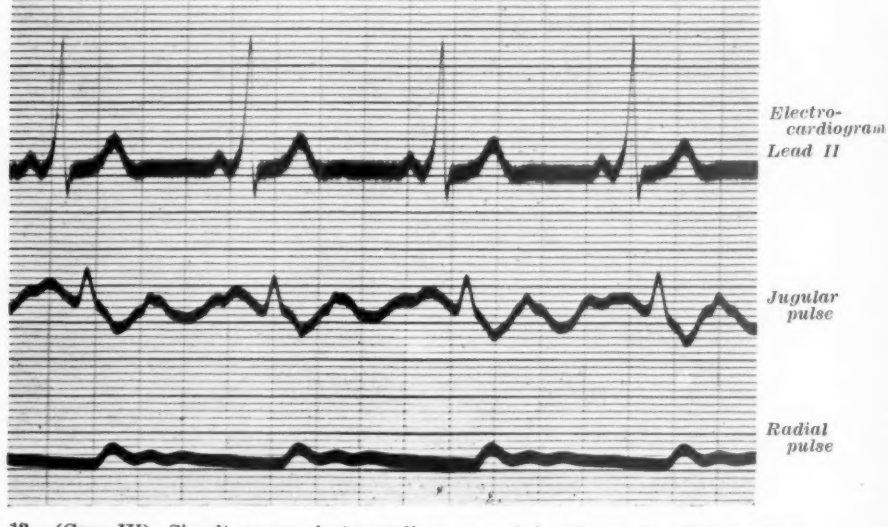


Fig. 12.—(Case IV) Simultaneous electrocardiogram and jugular and radial tracings. Bundle-branch block curves are present. The a. c. v. h. sequence is normal.

*Electrocardiograms.* Two distinct forms of curve were obtained, one replacing the other spontaneously as shown on successive plates (Figs. 9, 10 and 11). Figure 10 shows normal physiological complexes in all leads, P-R interval 0.15 second. Figure 11 shows a special form of complex with identical normal P-waves, shortened P-R interval (less than 0.1 second), and widened QRS complexes. The respective rates are much the same, the normal about 104, the abnormal about 108 a minute.

On January 20, 1926, the abnormal type of curve was constant, and simultaneous electrocardiogram and jugular and radial tracings showed a normal a.c.v.h. sequence (Figure 12).

On February 10, 1928, the normal type of electrocardiogram was constant.

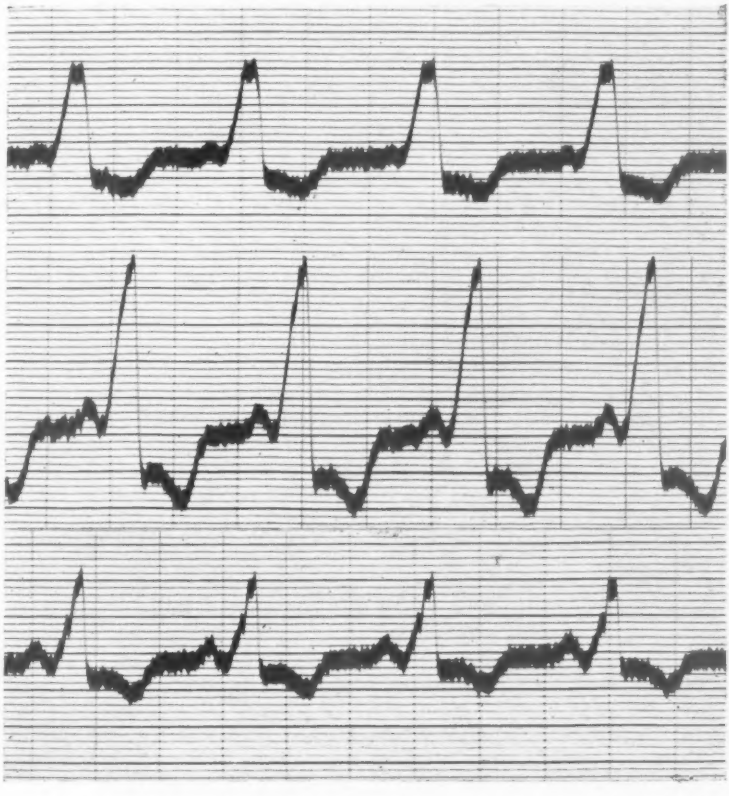


Fig. 13.—(Case V) Intraventricular block. The P-waves are normal and upright in all leads. The P-R interval is well under 0.1 second.

On October 10, 1929, the patient was examined again. He was able to play football and other games, but occasionally the heart would race at a high rate (about 200 per minute) for a few minutes. This would occur generally on exertion but once it took place in church. The electrocardiogram was now of the abnormal type.

On December 12, 1929, records showed the heart alternately in and out of the abnormal rhythm during several minutes, then the normal rhythm ruled. He was still fit and well apart from occasional attacks of palpitation.

*Case V.* G.H.K., male, aged 23 years when first seen by us on July 2, 1929. He complained of palpitation and slight pain in the left axilla. Once while in bed

the heart suddenly beat rapidly for a few minutes; similar attacks of palpitation occasionally occurred during the day. He played tennis and was not breathless on exertion. There was no rheumatic history.

*Examination* revealed no abnormal signs. The heart rate was 100 per minute. At this rate the blood pressure was 160 mm. mercury systolic, and 90 diastolic; at other times it was lower.

*Radioscopy* showed no cardiac enlargement.

*Electrocardiograms* were first taken in May, 1929, by Dr. Donald Hall of Brighton, to whom we are indebted for permission to publish the case. Our record

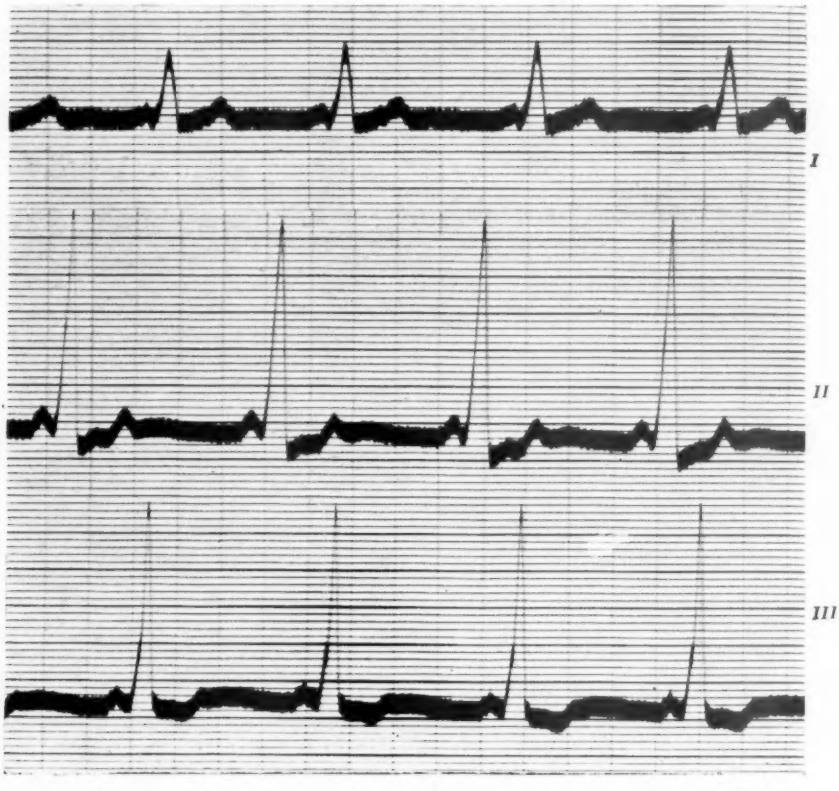


Fig. 14.—(Case VI) Intraventricular block. The P-waves are normal and upright in all leads. The P-R interval is well under 0.1 second.

of July 2, 1929, is similar (Fig. 13). The P-waves are normal and upright in all leads. The P-R interval is well under 0.1 second. The QRS complexes are wide and notched, and the T-waves are inverted in all leads.

This man was advised to continue his work as a market gardener.

*Case VI.* H.R.L., male, aged 23 years when first seen by us on October 8, 1928. He complained of palpitation and of slight breathlessness on exertion. At the age of 6 years he had enteric fever. There was no rheumatic history. At the age of 16 years the heart was found to be beating very rapidly and a doctor said it was enlarged. His games were restricted. Between the ages of 18 and 21 years, he was doing heavy manual work abroad without much distress. He was then rejected on medical examination, though he had only minor symptoms.

*Examination* revealed no abnormal signs. The heart rate was 80 a minute. The blood pressure was 130 mm. mercury systolic, and 85 diastolic.

The *orthodiagram* was normal.

*Electrocardiograms* showed abnormally widened ventricular complexes, regular at 60 per minute (Fig. 14). The P-waves were normal and upright in all leads. The P-R interval was just under 0.1 second. The next day, October 9, 1928, similar electrocardiograms were obtained. He was advised to disregard his occasional palpitation, but to find lighter work in view of the slight dyspnea on exertion. He proceeded abroad again.

In August, 1929, he was reported to be quite well and at work.

*Case VII.* B.H., male, aged 11 years when first seen by us April 13, 1929. There was a history of exhaustion, occasional pallor, and a varying pulse rate, often slow. He was always easily tired, and for a year he had had recurrent attacks in which he was pale and the pulse rate varied between 40 and 65 over a period of a few

Fig. 15.—(Case VII) Left bundle-branch block. The P-waves are normal and upright in all leads. The P-R interval is well under 0.1 second.

days. Otherwise he was fairly well and fond of games including football. Dyspnea had not been noticed. There was no rheumatic history.

*Examination* showed a smallish child, weighing 56 pounds; otherwise he looked well. The pulse rate was from 50 to 60 a minute and sinus arrhythmia was noted. The blood pressure was 110 mm. mercury systolic, and 75 diastolic. The heart sounds were normal and no murmurs were heard.

An *orthodiagram* showed a heart of normal size and shape.

*Electrocardiograms* on April 13, and again on April 16, 1929, were of the same form (Fig. 15). The P-waves were small and upright in all leads. The P-R interval was well under 0.1 second. The ventricular complexes had the form of left bundle-branch block.

*Case VIII.* C.B., female, aged 16 years when first seen by us on January 15, 1925. There was a history of alleged heart trouble. She had been quite well until two years before when she began to be obviously breathless at dancing and hockey. One night she felt a throbbing in her neck which kept her awake. She had im-

proved since two years ago and scarcely considered herself breathless. There was no rheumatic history.

*Examination* showed a girl of healthy color and appearance. There were bright red birthmarks on the left leg. There was no clubbing of the fingers. The heart sounds were normal. The blood pressure was 110 mm. mercury systolic, and 75 mm. diastolic.

*Radioscopy* showed slight to moderate enlargement of the heart to the right, with active systolic pulsation of the right and left borders; the diaphragm moved well.

A brisk walk with the patient showed that she was more breathless than a healthy observer.

*Electrocardiograms* showed a regular rhythm at a rate of from 60 to 70 a minute (Fig. 16). The P-waves were normal and upright in all leads. The P-R interval

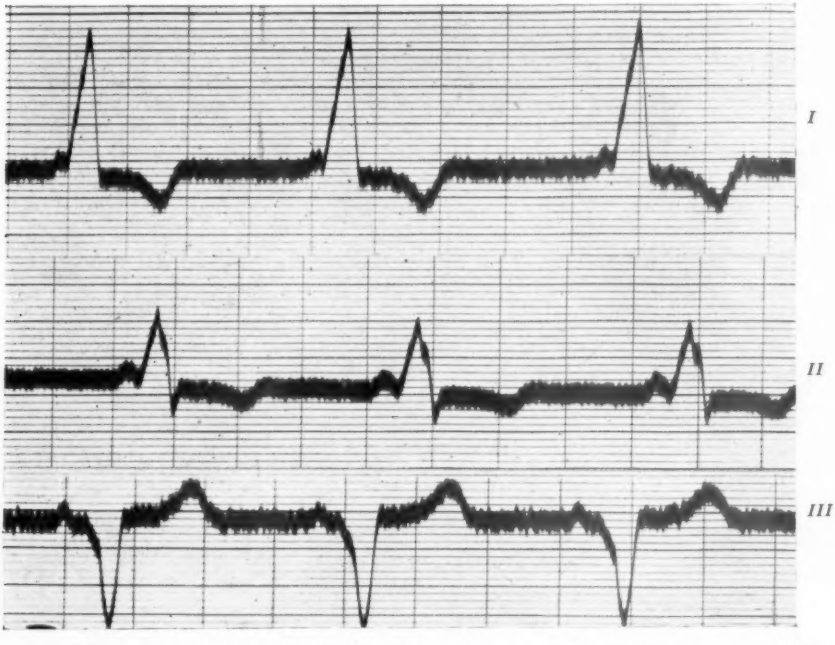


Fig. 16.—(Case VIII) Right bundle-branch block. The P-R interval is well under 0.1 second.

was well under 0.1 second. The ventricular complexes had the complete characteristics of right bundle-branch block. On January 16, 1925, the following day, exactly similar records were obtained.

Three years later, at the age of 19, she was reported to be in good health and hard at work as a student.

Recently (October 11, 1929) she has been seen again, at the age of 21 years. She is a university student, and is active and well. Her only complaint is that she is easily tired. Physical examination and radioscopy show no abnormalities. The electrocardiogram is now normal (Fig. 17) in contrast with that taken in 1925 (Fig. 16).

*Case IX.* H. H., male, a musician, aged 42 years when first seen at the London Hospital on the 28th of May, 1914. He complained then of attacks of palpitation, which began at the age of nine years. They were sudden in onset and offset, and

their duration varied from a few minutes to two weeks. Frequently the attacks could be stopped if the patient held his breath or put his head between his knees. Otherwise he was well.

There was no rheumatic history. He had diphtheria and scarlet fever some years after the onset of the attacks of paroxysmal tachycardia.

*Examination* when first seen, which was on the tenth day of an attack of

Fig. 17.—(Case VIII) Three years later. Normal physical curves. The P-R interval is 0.16 second. The P-waves are identical in Figs. 16 and 17.

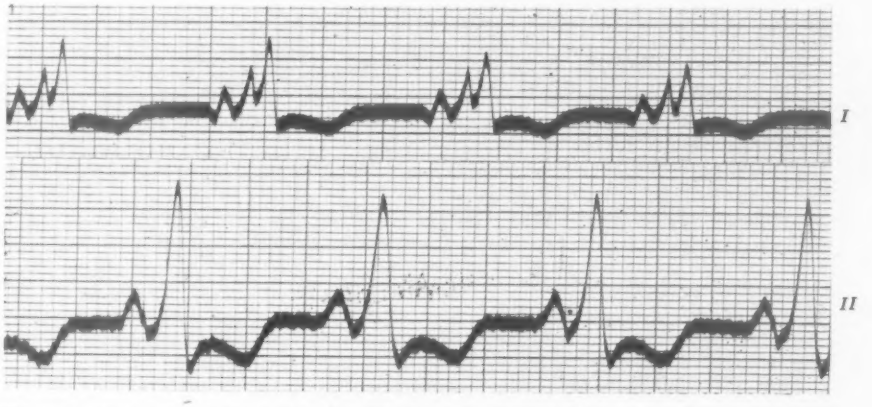


Fig. 18.—(Case IX) Intraventricular block. The P-R interval is 0.1 second. Time intervals = 0.2 and 0.04 seconds.

paroxysmal tachycardia showed dyspnea, a large heart, dulness and crepitations at the lung bases, and a large pulsating liver. The blood Wassermann reaction was negative.

*Electrocardiograms* taken after the paroxysm ended showed a regular rhythm with upright P-waves in all leads, a short P-R interval, abnormally widened QRS complexes and inverted T-waves in all leads (Fig. 18). An electrocardiogram was

obtained during a paroxysm of tachycardia at a rate of 150, the form of the curve being unlike that between attacks.

He was examined again on the 15th of September, 1914. The last paroxysm had occurred six weeks before and lasted three weeks. There was cardiac enlargement both on physical examination and by radioscopy. There were no murmurs. The lungs were normal.

Between the ages of 47 and 57 years he had no attacks. In 1928 the paroxysms returned. The heart was enlarged (radioscopy). An electrocardiogram between attacks was in general like that taken in 1914, as was another obtained during a paroxysm.*

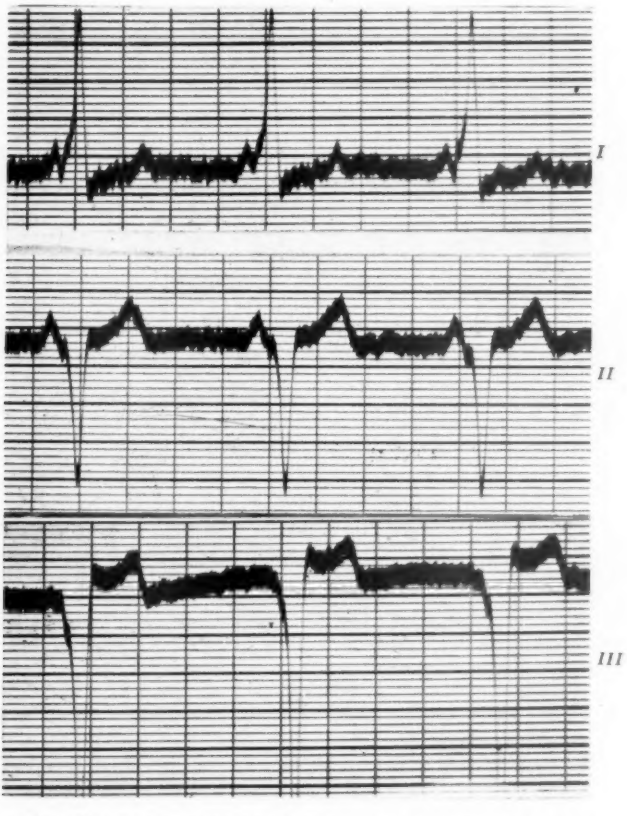


Fig. 19.—(Case X) Intraventricular block. The P-R interval is 0.1 second.

*Case X.* Mrs. A. C. M., a widow, aged 44 years when first seen in the Out-Patient Department of the Massachusetts General Hospital on November 26, 1927. She complained of attacks of palpitation. The attacks, which began at the age of 7, were always sudden in onset and offset. For the three years from 1924 to 1927 they had occurred more frequently, often daily. They lasted from a few minutes to several hours (intermittently) and were easily terminated by taking a deep breath and holding it, or by lying down.

*The patient's present condition has been described recently in a paper by Dr. Francis Bach entitled, "Paroxysmal Tachycardia of 48 Years' Duration, and Right Bundle-Branch Block." Proc. Roy. Soc. Med. London, 22: 412, 1929.

She had measles and diphtheria at the age of 5 years. In 1923 she had had her tonsils removed because of recurring tonsillitis and peritonsillar abscess. There was no rheumatic history.

*Physical examination* was entirely negative. The blood pressure was 140 mm. mercury systolic, and 85 diastolic.

*Electrocardiograms* showed a regular rhythm at the rate of 65 a minute (Fig. 19). The P-waves were normal and upright, and the P-R interval was 0.1 second. The ventricular complexes were of the type designated as indicating right bundle-branch block.

She was again seen on December 29, 1927, in an attack of paroxysmal tachycardia. The heart rate was over 200 and regular. An electrocardiogram was taken which showed auricular paroxysmal tachycardia at a rate of 230, without A-V block.

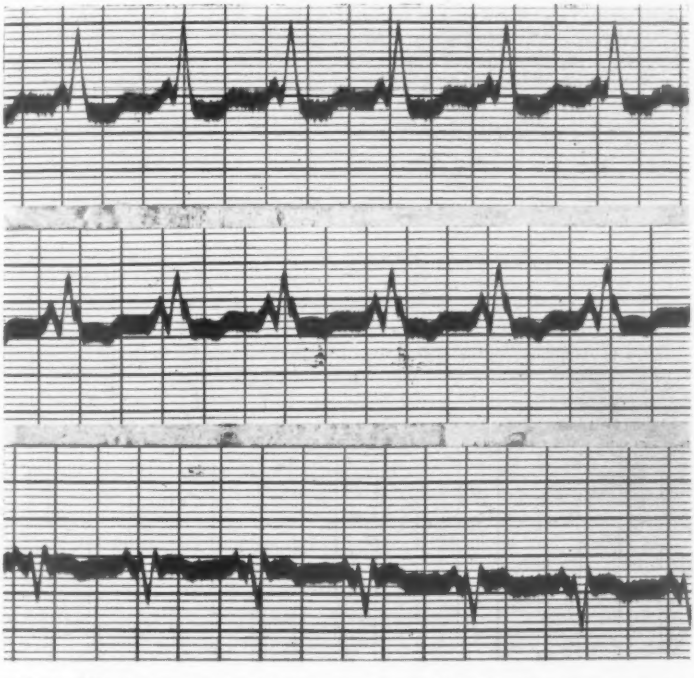


Fig. 20.—(Case XI) Intraventricular block. The P-R interval is less than 0.1 second.

The ventricular complexes were normal in form. After the electrocardiogram was taken she ended the attack by a forced inspiration. She then had frequent premature beats. She stated that since taking quinidine the attacks had become less frequent.

*Case XI.* Mrs. R. E., aged 55 years, entered the West Medical Service of the Massachusetts General Hospital on February 26, 1918, complaining of palpitation. The attacks of palpitation had begun ten years previously, but for the past four years the attacks had been somewhat more severe, occurring with change of weather to wet and cold, as well as after any indiscretion in diet. For two months prior to entrance into the hospital attacks of palpitation had been occurring at night, waking her out of sleep. As a rule the attacks lasted ten minutes.

There was no rheumatic history. She had had tonsillitis every year during youth. For a year there had been slight localized edema of the legs. She considered herself nervous.

Physical examination showed a poorly nourished, cyanotic, uncomfortable woman. The heart was moderately enlarged, the systolic blood pressure varied between 175 and 205 mm. mercury, the diastolic between 95 and 105. There was a loud apical systolic murmur transmitted to the axilla. There were signs of pulmonary tuberculosis.

The blood Wassermann reaction was negative.

*Roentgen ray examination* showed cardiac enlargement and pulmonary tuberculosis.

The *electrocardiogram* revealed normal P-waves which were upright in all leads. The P-R interval was less than 0.1 second. The ventricular complexes were of the type designated as indicating bundle-branch block (Fig. 20). The rhythm was regular and the rate 114.

## DISCUSSION

The combination of bundle-branch block, abnormally short P-R interval, and paroxysms of tachycardia (also paroxysmal auricular fibrillation and perhaps flutter) in young, healthy patients with normal hearts is distinctive, and worthy of recognition as a mechanism heretofore undescribed as such. The reversion to normal ventricular complexes and longer (normal) P-R interval, spontaneously or by vagal release following exercise or atropinization is characteristic. The paradoxical effect of vagal stimulation on the P-R interval is noteworthy.

We have been unable to demonstrate structural heart disease in our patients, except in the two oldest ones. One of these (Case IX) was first seen at the age of 42 years; he then had had paroxysms of tachycardia for 33 years. An electrocardiogram showed bundle-branch block with abnormally short P-R interval. Fourteen years later his electrocardiogram was essentially unaltered. The abnormal cardiovascular signs on physical examination in this patient may have been the result of coincidental development of organic heart disease. The other patient (Case XI) was 55 years old when first seen, and on account of her age and the presence of hypertension, we believe that the abnormal cardiovascular signs were probably coincidental and not associated with the peculiar mechanism, already described, present in this case.

None of our patients presented evidence or gave a history of rheumatic infections. Other infections, toxic states, and rapid heart rates were not responsible for the abnormal electrocardiograms. The subjects were in good health, and as a rule the only complaint was palpitation. The age of our patients suggests that a congenital anomaly may be responsible for the phenomena observed in this group. We have no proof for or against this suggestion. All the available evidence points to vagal influence as the controlling factor in this mechanism. Incidentally, it may be pointed out that here is a group of patients in whom paroxysmal tachycardia and auricular fibrillation (and perhaps flutter) is obviously associated with this unusual mechanism, quite possibly of vagal origin.

A case undoubtedly exhibiting the same mechanism was described in 1921 by A. M. Wedd.[6] A student, 19 years old, had had paroxysms of

tachycardia since the age of 5 years. He was well otherwise and the heart and blood pressure were normal. Electrocardiograms showed intraventricular block and a P-R interval of 0.08 second. The P-waves were upright in all leads. At other times the ventricular complexes were normal, and the P-R interval doubled. The author assumes the presence of A-V nodal rhythm.

A somewhat similar case was reported by F. N. Wilson in 1915.[1] This patient had mitral stenosis, and the author suggests that it is "improbable that the bundle-branch block was due to vagus influence alone," but that "conduction through the right branch of the A-V bundle was already impaired and that this rendered it especially susceptible to vagus influence." The short P-R interval was explained by assuming that A-V nodal rhythm was present; the P-wave was inverted in Leads II and III.*

A study of the electrocardiograms of our patients has enabled us to exclude the presence of A-V nodal rhythm because frequent ventricular premature beats were followed consistently by compensatory pauses, and the form of the P-waves occurring with both long and short P-R intervals was identical. In several patients the P-waves were distinctly notched, making identification easy and certain. Finally, the P-waves were always upright in all three leads.

The group includes eight males and three females. The youngest patient was eleven years old when first seen. Two patients were 16, one 18, one 21, two 23, one 35, and the three oldest patients were 43, 44 and 55 years respectively. One patient had attacks of paroxysmal tachycardia for 48 years, another for 37 years, one for 14 years, and two patients for 10 years respectively.

## SUMMARY AND CONCLUSIONS

1. Eleven cases are here reported of an unusual cardiac mechanism, heretofore undescribed as such, consisting of functional bundle-branch block and abnormally short P-R interval, occurring mostly in otherwise healthy young people with paroxysms of tachycardia or of auricular fibrillation.

2. Spontaneously, or following release of vagal tone by exercise or atropinization, the ventricular complexes revert to the normal physiological form, and the P-R interval lengthens to become normal.

3. Vagal influences seem to be largely responsible for the mechanism described. A paradoxical effect of vagal stimulation on the P-R interval has been observed.

4. Infection, rheumatic and otherwise, toxic states, and rapid heart rates are not responsible for the abnormal electrocardiogram. Auriculo-

*Recently W. W. Hamburger in the Medical Clinics of North America (13: 343, 1929) reported the occurrence of bundle-branch block with a short P-R interval in a child aged four and one-half years, who had had paroxysmal tachycardia for one year. The author assumed that acute severe right bundle-branch block occurred as the result of an acute respiratory infection.

ventricular nodal rhythm is apparently not responsible for the short P-R interval.

5. From a study of the cases here presented we conclude that:

a) Aberrant ventricular complexes of the type generally recognized as indicating bundle-branch block may occur in healthy people with normal hearts.

b) Vagal stimulation is capable of altering markedly the form of the ventricular complex, and may be responsible for the occurrence of complete bundle-branch block curves in apparently normal hearts at normal rates of beating.

c) Vagal stimulation may shorten markedly the P-R interval without the production of A-V nodal rhythm, and without dislocating the auricular pacemaker.

d) In the group of cases reported paroxysmal tachycardia and auricular fibrillation are associated with the nervous control of the heart.

e) The recognition of functional bundle-branch block is of considerable practical importance. The combination of intraventricular block with abnormally short P-R interval, interchangeable with normal ventricular complexes with longer P-R interval (reversion spontaneous or following exercise or atropinization) in healthy young people with paroxysmal tachycardia (or auricular fibrillation) is distinctive.

f) This mechanism is apparently not indicative of disease of the heart.

NOTE: In this paper bundle-branch block when mentioned is referred to according to the old nomenclature of right bundle-branch block for upright widened Q-R-S waves in Lead I and inverted widened Q-R-S waves in Lead III, and left bundle-branch block for inverted widened Q-R-S waves in Lead I, and upright widened Q-R-S waves in Lead III according to the newly revised nomenclature, which is probably correct, these designations would be changed, so that one should read "left bundle-branch block" for "right" and "right bundle-branch block" for "left" in this paper.

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# THE SUBSEQUENT COURSE AND PROGNOSIS IN CORONARY THROMBOSIS

## An Analysis of 287 Cases*

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WITH a growing understanding of the clinical picture of acute coronary closure it has become increasingly evident that a considerable proportion of such patients survive their first attack and that some of these thereafter enjoy reasonably good health for a good many years. It was in the hope of throwing some further light upon the fate of such patients as have lived through one attack that this study of a large number of cases of coronary thrombosis was undertaken.

The material for this study has been assembled from three different sources: the private records of one of the writers (117 cases); the two medical services of the New York Hospital† (119 cases); and the medical department of the Out-Patient Clinic of the Cornell Medical College (51 cases). It has seemed probable that material gathered from these three sources would present a fairly accurate picture of the disease as it is seen in the different social and economic strata of the community.

Although the diagnosis in most of the cases was not confirmed by autopsy (there were 31 autopsies among the 48 patients dying in the hospital), we feel quite certain that only cases with acute coronary closure and cardiac infarction have been included in this study. Cases in which there seemed the slightest doubt as to the accuracy of the diagnosis have been excluded. This statement applies especially to the so-called atypical clinical types in which pain is usually an inconspicuous feature. Only one case presenting the picture of acute pulmonary edema has been included, and in that instance the diagnosis was confirmed by necropsy. On the other hand it seems reasonably certain that by following this rule strictly a considerable number of genuine instances of thrombosis have been rejected. After all there are few diseases which offer more opportunities for the ultimate confirmation of the clinical diagnosis, even without autopsy, than does the one under consideration.

### SEX

Among the 287 cases analyzed 243, or 84.7 per cent occurred in men and 44, or 15.3 per cent, in women. This ratio corresponds fairly well

*Read at the meeting of the Association of American Physicians at Atlantic City, May, 1930.

†The authors are greatly indebted to Dr. W. R. Williams for permission to include in this study, cases from the Second Medical Division of the New York Hospital.

with that of other statistics and with the generally accepted view that the disease is many times more frequent in men than in women.

### AGE AT FIRST ATTACK

An analysis of the age incidence at the time of the first attack was begun rather as a perfunctory duty and without any expectation that the figures would disclose anything of special interest, but it soon became apparent that the tabulation revealed facts which were both surprising and suggestive. It should be emphasized that the figures given represent the age at the time of the first attack and not necessarily that at the time of the attack in which the patient was seen. Such statistics we believe have hitherto never been presented.

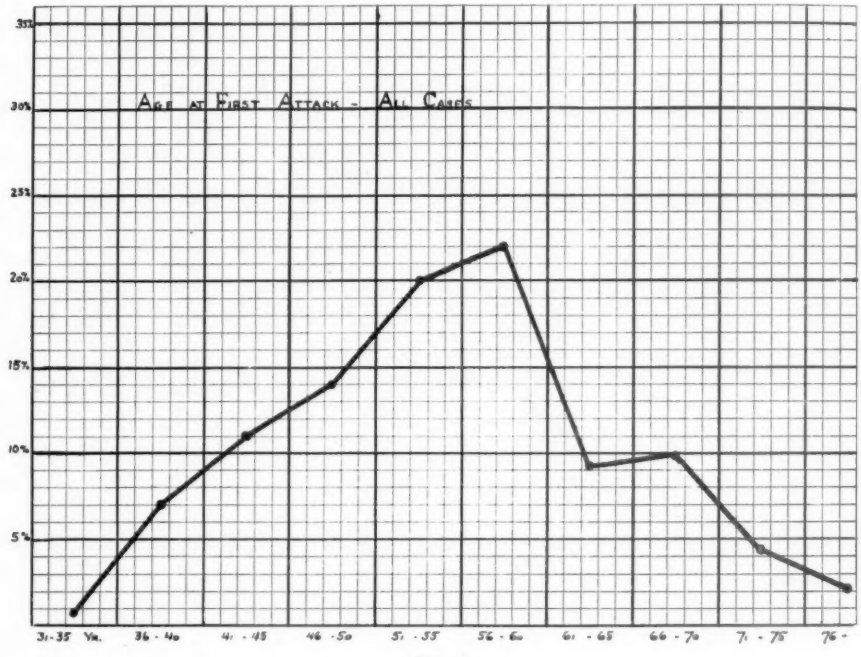


Fig. 1.

In Fig. 1 are plotted, in percentages of the total number, the ages of all the patients arranged in five-year periods. It will be seen that the curve of incidence rises steadily and almost uniformly from the 31-35 year period to reach its maximum height in the 56-60 year period, after which it falls very abruptly. Furthermore it will be seen that 75 per cent of the patients have had their first attack before the sixty-first year and only 25 per cent after that time; that the incidence is distinctly greater in the 41-45 year period than in either of the five-year periods in the decade between 60 and 70, and that the percentage of cases having their onset in the 36-40 year period is considerably greater than that having their onset in the years between 71 and 75. These figures seem

to point conclusively to the fact that coronary thrombosis is a disease which usually has its onset, not in the later years of life, but rather in the years between 40 and 60. In encountering instances of undoubted coronary thrombosis in the decade between 40 and 50 it has been customary to look upon them as distinct exceptions to the general rule. In the present series, however, no less than one-third of all the patients had their first attack before the fifty-first year; and one is forced to conclude, if this series can be accepted as representative, that such precocious cases constitute an important fraction of the whole number and cannot be regarded as in any way exceptional.

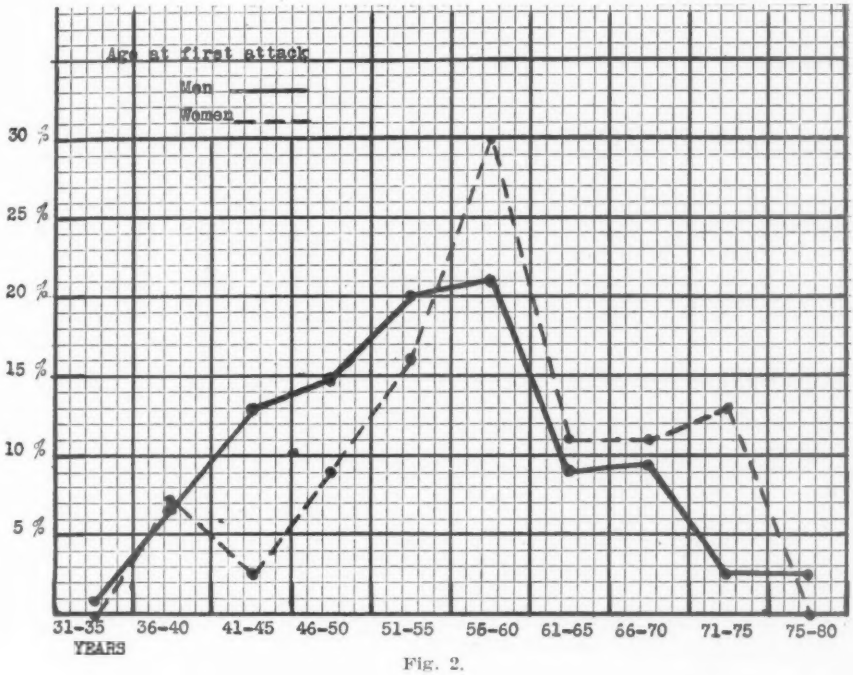


Fig. 2.

If then one assumes that local arteriosclerotic changes in the coronary arteries or their branches represent an essential factor in the production of thrombosis, the conclusion seems unescapable that, often at least, visceral arteriosclerosis must begin at a much earlier age than we have been accustomed to believe. Although not directly pertinent to the subject of the paper, this evidence pointing to the frequency of sclerotic changes in the coronary branches in early middle life seems to the writers one of the most important and most suggestive facts that this analysis has brought to light.

### COMPARISON OF AGES AT FIRST ATTACK OF MEN AND OF WOMEN

In Fig. 2 are plotted separately the age incidences in five-year periods of the first attack in men and in women. It will be seen that

whereas the curve for men, as was to be expected, corresponds very closely with that for all the cases (Fig. 1), the curve for women shows distinct differences. There is a noticeable lag in the curve during the earlier five-year periods, a sudden sharp peak (30 per cent) in the 56-60 year period and a distinctly greater proportion of cases in the later years of life.

### ASSOCIATION OF CORONARY THROMBOSIS WITH ARTERIAL HYPERTENSION, SYPHILIS AND DIABETES

Among the 274 patients in whom the information was available, preexisting disease, in the form of arterial hypertension, syphilis or diabetes, was recorded as follows:

Arterial hypertension in 93 cases, or 33.9 per cent.
Syphilis (proved or probable) in 39 cases, or 14.2 per cent.
Diabetes in 28 cases, or 10.2 per cent.

In view of the widespread belief that persistent high blood pressure is much the most important predisposing factor to coronary disease, the low figure given above for hypertension (34 per cent) will come as a surprise to many. Without insisting upon the accuracy of these figures (since they represent only those patients *known* to have had preexisting hypertension) it nevertheless seems reasonably certain that such hypertension cases made up, at the most, not more than half of the total number. In the series of 100 cases reported by Parkinson and Bedford[1] there were 15 patients with an antecedent systolic blood pressure of 200 mm. or over and 34 patients with systolic pressures ranging between 150 and 200 mm.—a total of 49 per cent. Among the 145 patients studied by Levine,[2] 58 (or 40 per cent) were known to have had an antecedent hypertension. Nevertheless Levine concludes "that a distinct hypertension existed as a forerunner of coronary thrombosis in the majority of cases"; basing this conclusion upon the fact that "many patients with normal blood pressures showed retinal changes of a sufficiently well marked degree to indicate that a previous hypertension had existed."

We, ourselves, have for a long time been much impressed by the frequency with which coronary thrombosis appears in individuals whose blood pressures have remained *low* and have failed to show the usual tendency toward gradual increase with increasing years, and we have formed the impression that the disease is to be found among such persons almost as frequently as among those with hypertension. In the present series the records available are not sufficiently full either to confirm or to disprove that impression.

COMPARISON OF AGES AT FIRST ATTACK OF HYPERTENSION CASES WITH THOSE FOR ALL CASES

In Fig. 3 are plotted separately the percentages of age incidence, in five-year periods, of cases of pre-existing hypertension and of all cases. The curve for the hypertension cases, as compared with that for all cases, shows a distinctly smaller incidence in the five-year periods up to and including the 51-55 year period, and a somewhat increased incidence in the 66-70 year period.

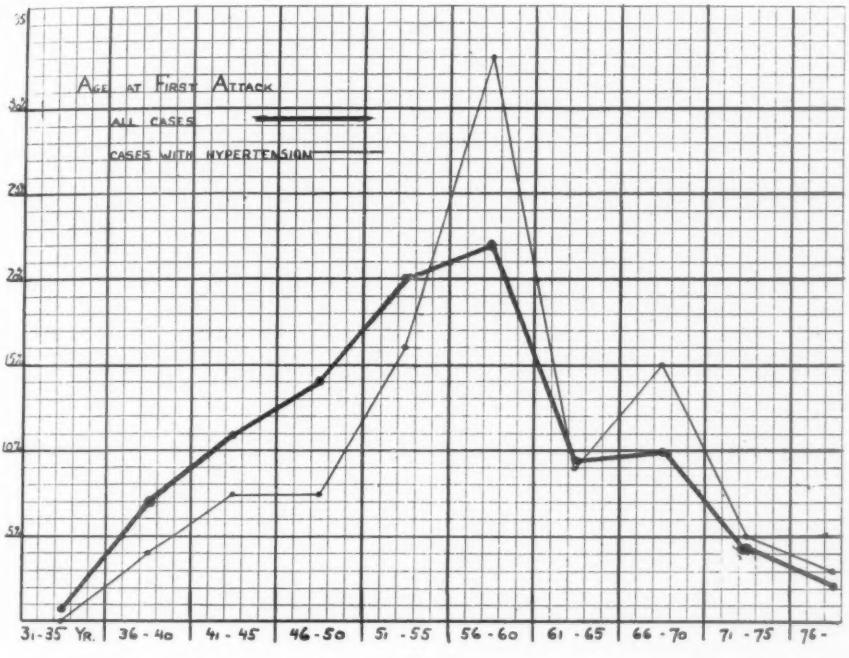


Fig. 3.

COMPARISON OF AGES AT FIRST ATTACK OF CASES WITH SYPHILIS WITH THOSE FOR ALL CASES

Syphilis, either proved or probable, was found in 39 patients, or 14.2 per cent of 274 patients. The "proved" cases included those with either definite physical signs of syphilis or with a clear history of that disease. Patients in whom there was only a positive Wassermann reaction were classed as "probable." Fig. 4 shows the graph of the age incidences of the first attack in cases with syphilis in comparison with that for all cases. Although the differences between the two are not great, there is among the syphilitic cases an appreciable shift of the curve toward the earlier age groups. How significant this shift may be is questionable in view of the fact that in most instances, even among the cases with syphilis, we have no proof that the lesions in the coronary vessels were actually of a luetic nature. Certainly the earlier belief that

the precocious cases of coronary thrombosis usually have a syphilitic basis is no longer tenable, for in most of the early cases in this series there was no evidence whatever of an antecedent luetic infection.

### COMPARISON OF AGES AT FIRST ATTACK OF CASES WITH DIABETES WITH THOSE FOR ALL CASES

Trustworthy evidence of a pre-existing diabetes at the time of the first attack of coronary thrombosis was obtained in only 28 patients, or 10.2 per cent of 274 cases. This figure was unexpectedly low, and it seems probable that it is below the true incidence of that disease as it

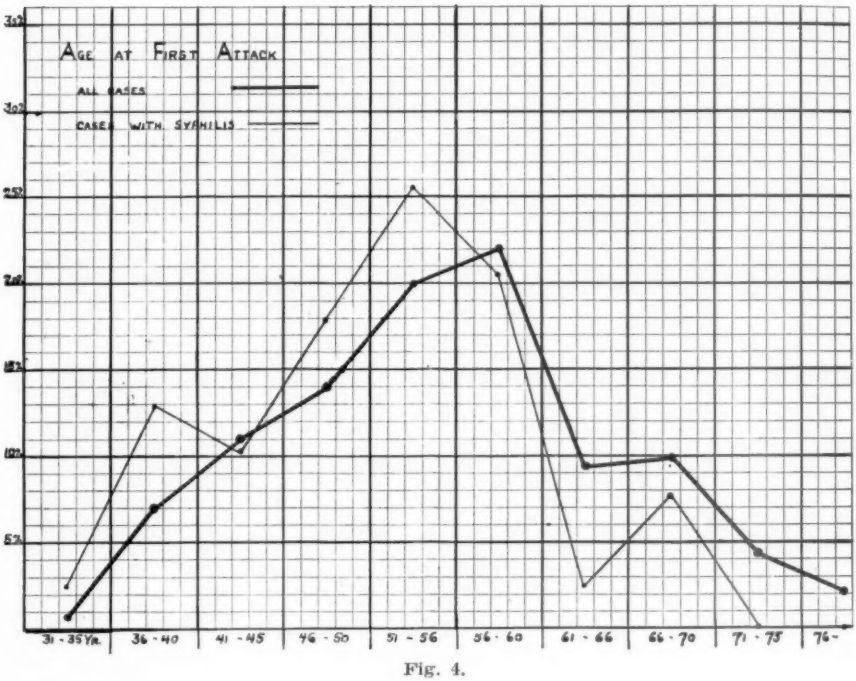


Fig. 4.

is found associated with coronary thrombosis. It is quite probable that in some instances a more thorough investigation might have revealed a latent diabetes. Levine, in his series of 145 cases of coronary thrombosis, found evidence of diabetes in 34 cases, or 23.7 per cent.

In Fig. 5 is plotted, by five-year groups, the age incidence at the time of the first attack, of the cases complicated by diabetes in comparison with that for all cases. The small number of cases with diabetes renders such a comparison of doubtful value, but the chart shows an interesting concentration of the diabetic cases in the age groups between 50 and 60 years, and a correspondingly smaller percentage of cases in the earlier and later age groups. Just what the significance is of this association of diabetes with coronary disease is still uncertain. It

seems probable, however, that diabetes is not, in itself, a predisposing cause of coronary thrombosis but that both of these conditions are the separate expressions of a single underlying cause—visceral arteriosclerosis.

## GENERAL STATISTICS

Before taking up a detailed analysis of the fate of the patients included in this study, it is desirable to present a few general statistical figures. Of the 287 patients whose records were reviewed, 117 are known to be living at the present time and 142 are known to have died. In the case of the remaining 28 patients, it has been impossible to trace

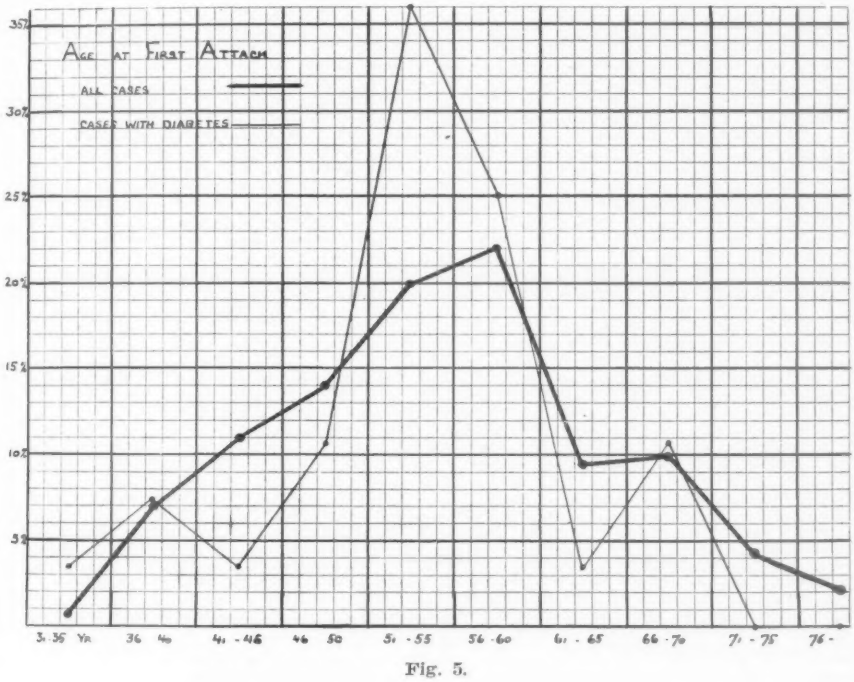


Fig. 5.

them, and their fate is unknown. That is to say, of the 259 patients concerning whom there is definite information, 45 per cent are living and 55 per cent have died. Three patients in their first attack left the hospital as soon as the severe pain had subsided and have been lost, so that it is not known whether they survived even their initial attack. Of the 142 patients who have died, 46 succumbed during their first attack. This gives an immediate mortality in the initial attack of 16.2 per cent* (of 284 cases). This percentage of deaths in the first attack is surprisingly low—much lower than is usually represented. Among

*In estimating the immediate mortality we have included all patients who died within one month of the onset of the attack and a few also who survived a week or two beyond this period but who continued gravely ill throughout all that time.

Levine's cases the immediate mortality in an attack was 53 per cent, but no statement is made as to the mortality in the first attack alone.

### COMPARISON OF AGES OF THOSE WHO DIED IN THE FIRST ATTACK AND OF THOSE WHO MADE A GOOD RECOVERY

In order to determine if the age of the patient at the time of the first attack bore any important relation to the outcome of the attack, the age incidence, in five-year periods, of those who died in the first attack and of those who recovered and remained well for some time is

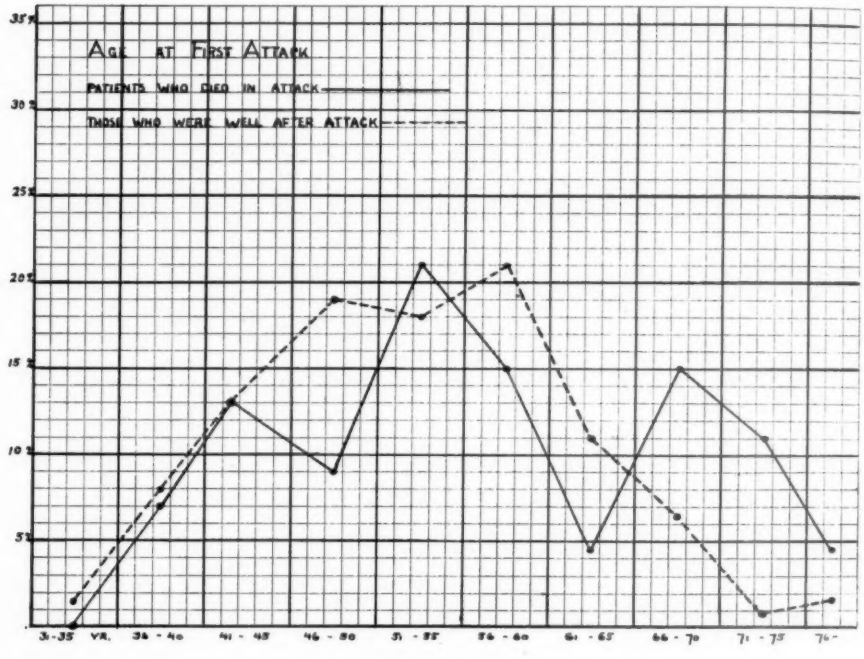


Fig. 6.

plotted separately in Fig. 6. It cannot be said that this comparison brings out any very convincing facts except that in the later age groups —from 66 years on—there is a disproportionately large percentage of the fatal cases and a small percentage of the patients who recovered and remained well.

### RELATION OF THE IMMEDIATE PROGNOSIS TO THE SEVERITY OF THE SYMPTOMS OF THE ATTACK

In an effort to learn whether or not the outlook for immediate recovery from an attack bears any close relation to the intensity of the symptoms of the attack, all the cases (172) in which the data were sufficiently complete were divided arbitrarily into three groups, representing different degrees of severity of the initial symptoms of the attack. The criteria for this grouping, which necessarily is only a crude

one, were the intensity and the duration of the pain, the degree of dyspnea, and the severity of the shock—as indicated by the pallor, sweating, vomiting, fall of blood pressure and changes in the pulse. The results of this analysis are shown in Table I. It will be seen that

TABLE I

RELATION OF IMMEDIATE PROGNOSIS TO SEVERITY OF SYMPTOMS OF ATTACK (IN 172 CASES)

| | DIED | | RECOVERED | |
|---|---|---|---|---|
| Severity | Number | Per Cent | Number | Per Cent |
| +++ | 28 | 68 | 41 | 31 |
| ++ | 9 | 22 | 56 | 43 |
| + | 4 | 10 | 34 | 26 |
| Total | 41 | 100 | 131 | 100 |

among the fatal cases rather more than two-thirds had symptoms classed as very severe (+++), and only 10 per cent had symptoms classed as mild (+). On the other hand among the patients who recovered from the attack, 31 per cent had symptoms rated as very severe, and 26 per cent those rated as mild. In other words, although the immediate prognosis is certainly worse among patients having extremely severe initial symptoms, nevertheless almost one-third of those who recovered had symptoms of that character.

### KNOWN DURATION OF PERIOD OF GOOD HEALTH AFTER FIRST ATTACK

Among patients who have made a good recovery from the first attack of coronary thrombosis, one of the very important points in prognosis is to know what may be considered to be their expectancy for good health. We have attempted to reach a rough approximation of such expectancy by tabulating the duration of good health in 89 patients who are still alive and well, and by including also 28 patients who are now dead but who were in good health up to the time of a second attack. As the patients of the first group are still alive and well, it is obvious that the figures derived from their records must be below the true ones for health expectancy. In the case of the second and much smaller group, however, the figures are of course accurate. As used by us the term "good health" indicates a state of health which permits the patient to live his accustomed life and to regard himself as essentially well. Not all were entirely free from pain or other discomforts, but these symptoms were not sufficient to cause the patient to modify his mode of life or to prevent him from working. Table II, which is

TABLE II

KNOWN DURATION OF PERIOD OF GOOD HEALTH AFTER FIRST ATTACK (89 PATIENTS ALIVE, 28 WELL UP TO SECOND ATTACK, DEAD)

| 3 MO. | 6 MO. | 1 YR. | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12...17 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 109 | 101 | 88 | 65 | 49 | 40 | 25 | 17 | 15 | 7 | 4 | 4 | 3 | 2 | 1 | Patients (117) |
| 93 | 86 | 75 | 56 | 42 | 34 | 21 | 15 | 13 | 6 | 3.4 | 3.4 | 2.6 | 1.7 | 0.9 | Per cent |

made up from the records of 117 patients, has been arranged to show the number of patients, and the percentage of the whole, who were in good health at the end of the different time periods. Thus at the end of three months after the first attack 109 (93 per cent) of the 117 were still well; at five years 17 (15 per cent); at ten years 4 (3.4 per cent), and finally at the end of 17 years one patient was still alive and well. This plan of tabulation has seemed to us to give a truer picture of the health expectancy than would be gained by merely recording the average duration of good health for the group.

### FATE OF PATIENTS WITH ANTECEDENT CIRCULATORY SYMPTOMS

The relation between attacks of coronary thrombosis and an antecedent angina of effort has been so close that from the time of Heberden almost to the present time the clinical distinction between the two conditions has not been clearly recognized. Among the 274 patients of this series whose records were satisfactory upon this point, 105, or 38 per cent, had had antecedent anginal or other circulatory symptoms and 169, or 62 per cent, had had no such antecedent symptoms. In other words considerably more than half of all the patients had had no warning of any sort that would lead them to doubt the integrity of the heart.

In the group of cases presenting such antecedent circulatory symptoms the mortality in the first attack was 24 per cent, whereas that for all cases was 16.2 per cent. These facts appear in detailed form in Table III.

TABLE III

FATE OF PATIENTS WITH ANTECEDENT CIRCULATORY SYMPTOMS

| | | |
|---|---|---|
| 169 Patients had no antecedent symptoms | | 62 per cent |
| 105 Patients had antecedent symptoms | | 38 per cent |
| Angina of effort, few wk. to 10 yr. | 64 cases | |
| Dyspnea on effort | 24 " | |
| Angina and dyspnea | 11 " | |
| Claudication | 3 " | |
| Paroxysmal fibrillation | 2 " | |
| Paroxysmal tachycardia | 1 case | |

Of these, 25 died in first attack, 24 per cent
(Against 16.2 per cent of all cases)

### EFFECT OF ATTACK UPON ANGINAL PAIN

It has often been noted that occasional cases are seen in which troublesome anginal symptoms have ceased entirely after the successful ordeal of an attack of coronary thrombosis. In the group of patients having antecedent pain of a troublesome character and recovering satisfactorily from the first attack of coronary closure, there were 22 in whom this point could be satisfactorily investigated. In eight of the 22 patients anginal pain ceased with the attack of thrombosis and did not return. There were five patients in whom after the attack the pain

was worse than before. Two patients had less pain but were not entirely free, and in seven cases there was little or no change in the pain.

### NUMBER OF ATTACKS

With respect to the number of distinct attacks of coronary thrombosis undergone, the 287 patients included in this series may be grouped as follows:

| | | |
|---|---|---|
| Single attack | 190 patients | 67 per cent |
| Two attacks | 69 " | 24 " " |
| Three attacks | 12 " | 4 " " |
| More than three attacks | 14 " | 5 " " |
| Doubtful | 2 " | |

It must be understood that these figures have only a limited significance, for they are derived not only from the records of 142 patients who are dead but also from those of 117 patients who are still living and from those of 28 patients who cannot now be traced. It is certain therefore that, among the patients living, fresh attacks will occur in many if not in most of them, and that the true percentages would differ from those given above by showing a smaller percentage of single-attack cases and a larger percentage of cases with a record of two or more attacks.

### SINGLE-ATTACK CASES

Turning now to a study of the 190 patients who have had but a single attack, there were three who left the hospital as soon as the initial symptoms had subsided and of whom nothing further is known—not even whether or not they survived the first attack. The record of the other 187 cases may be summarized as follows:

| | | | |
|---|---|---|---|
| Living and well | 61 | (33 per cent of 187) | 50 per cent |
| Living but not well | 27 | | |
| Fate unknown | 11 | | |
| Died in attack | 46 | (16.2 per cent of 284) | 50 per cent |
| Died after attack | 42 | | |

If this group of single-attack cases be further analyzed, with reference to those patients, both living and dead, who were *not* well after the attack, it is found that of 69 cases of that sort satisfactory data are available in sixty. These, together with the time interval since their attack, may be classified as follows:

| | | |
|---|---|---|
| Living, fair health | 14 | (2 months to 3 years; average 10 months) |
| Living, poor health | 13 | (2 months to 2 years; average 8 months) |
| Dead | 33 | (1 month to 3½ years; average 12 months) |

The term "fair health" has been applied to those who had symptoms of a milder sort, such as anginal pain or dyspnea on effort, but who were able to lead a fairly normal life even though they were not well enough to work steadily. Most of the patients classed as having poor

health and as dead suffered from progressive cardiac failure. A few of those among the dead continued in fair health up to the time of their sudden death.

### TWO-ATTACK CASES

The statistics of the 69 patients who had two attacks of coronary thrombosis are as follows:

| | |
|---|---|
| Living and well after two attacks | 15 or 22 per cent |
| Living but not well | 5 |
| Fate unknown | 9 |
| Died in second attack | 20 or 29 per cent |
| Died after second attack | 20 |

Comparison of these figures with those for the first attack reveals that whereas after the first attack 33 per cent of the patients were "living and well," after the second attack only 22 per cent could be so classified, and that whereas only 16.2 per cent of the patients died in the first attack 29 per cent died in the second.

### INTERVAL BETWEEN FIRST AND SECOND ATTACKS

The interval of time which elapsed between the first and second attacks in 78 cases in which there were two or more attacks is shown in Table IV. In exactly half of the cases this interval was less than one

TABLE IV

INTERVAL BETWEEN FIRST AND SECOND ATTACKS (78 CASES)

| UNDER 3 MO. | 3-6 MO. | 6-12 MO. | 1-2 YR. | 2-3 YR. | 3-4 YR. | 4-5 YR. | 5-6 YR. | 6-7 YR. | 7-8 YR. | 8-9 . . . 18 YR. | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | 6 | 13 | 11 | 7 | 3 | 3 | 7 | 2 | 4 | 1 | 1 Cases |
| | 50 % | | | | | | | | | | |

year. Among the other half of the patients, however, the interval in many instances was very much longer and in one case was actually eighteen years.

### THREE-ATTACK CASES

There were twelve patients who had three attacks of coronary closure. Of these, six (50 per cent) are still alive and well; two died in the third attack; three died after the attack and one patient was lost. In these patients the intervals between the first and second attacks varied from one month to seven years, and the intervals between the second and third attacks from one month to five years. In one patient these intervals were respectively five years and five years; in another patient, seven years and four years.

### MULTIPLE-ATTACK CASES

Fourteen patients have had from four to seven distinct attacks of coronary thrombosis. Of these three are living (2½, 1¼, and 4½ years

after the first attack) and nine have died. The fate of two patients is unknown.

The patient who had seven attacks of coronary thrombosis was a physician who had his first attack at the age of 53 years and who died in the seventh at the age of 57. At the age of 42 years he had auricular fibrillation for several weeks following an appendectomy for acute suppurative appendicitis, and at the age of 45 years he again had auricular fibrillation, this time following an attack of influenza. Otherwise he had no cardiac symptoms until his first attack of coronary thrombosis in September, 1924. Subsequent attacks occurred in July, 1925, January, 1926, April, 1926, July, 1926, March, 1928, and June, 1928. These attacks were typical and severe and were accompanied by electrocardiographic changes. There was progressive diminution of cardiac reserve forcing a gradual restriction of activities. In November, 1927, there was an attack of nocturnal pulmonary edema, and four other attacks of pulmonary edema occurred during the following January and February.

## VASCULAR COMPLICATIONS

*Embolism.*—Attacks diagnosed as those of embolism, in which presumably the emboli arose from mural thrombi in either the left or the right ventricle, were recorded 49 times among 42 of the 287 patients. Of these attacks 28 involved the systemic arteries and 21 the pulmonary artery. The details are as follows:

| | |
|---|---|
| Cerebral | 14 |
| Renal | 8 |
| Mesenteric | 3 |
| Popliteal | 1 |
| Brachial | 1 |
| Retinal | 1 |
| | 28 |
| Pulmonary artery | 21 |

In two patients both systemic and pulmonary arteries were involved in the embolic attacks. Among the 42 patients concerned in the attacks of embolism, 27 recovered and 15 died—not necessarily, however, from the immediate effects of the embolic attack.

*Thrombosis.*—In considering the pathogenesis of coronary thrombosis the question often has been raised as to whether the chief determining cause was to be sought in the local arteriosclerotic process or rather in some constitutional thrombophilic tendency. In the records of the present series there is little to furnish support to the latter theory. Associated arterial thromboses are recorded in only two of the cases. In each of these there was the history of an antecedent cerebral attack, believed to be a thrombosis, and in each also a cerebral thrombosis many months after the attack of coronary thrombosis. In addition to these two cases of cerebral thrombosis there were four cases of venous throm-

bosis which manifested itself during or soon after the active symptoms of the cardiac attack. It seems probable that the advent of the venous thrombosis was determined rather by the sudden circulatory failure than by any constitutional tendency in that direction.

### ELECTROCARDIOGRAMS

One hundred and fifty-one of the patients had one or more electrocardiograms; these are not all comparable, because in some cases the records were taken only at the time of the acute attack and in others only at some later time. The electrocardiographic changes were not on the whole a reliable aid in prognosis, but in general patients with normal or nearly normal records did best while those with evidence of arborization block or of bundle-branch block did badly. It is evident that if electrocardiograms are to be of real value in prognosis they must be taken at frequent intervals from the time of the attack onward, and that it is the progressive changes in the form of the tracing rather than its appearance at any one time that is significant.

TABLE V

ELECTROCARDIOGRAMS IN 151 PATIENTS

| | PATIENTS | LIVING | DEAD | LOST |
|---|---|---|---|---|
| Normal or nearly normal records only | 26 | 14 | 7 | 5 |
| Changes in T-waves, with or without QRS change, not bundle-branch block | 109 | 37 | 52 | 20 |
| Heart-block, complete, 2:1 or dropped beats | 7 | 4 | 2 | 1 |
| Auricular fibrillation or flutter, transient or permanent | 19 | 5 | 10 | 4 |
| Bundle-branch block | 15 | 4 | 10 | 1 |

### SUMMARY

The records of 287 cases of coronary thrombosis have been studied with respect to the clinical course of the disease from the time of the first attack. Approximately 85 per cent of these cases were found in men and 15 per cent in women.

An analysis of the age incidence at the time of the first attack discloses the fact that in one-third of all the cases the first attack occurred before the fifty-first year, and in three-fourths of the cases before the sixty-first year. It seems evident therefore that coronary thrombosis must be regarded as essentially a disease of *early* middle life rather than of elderly life as it is usually held to be.

Evidence of an antecedent arterial hypertension was found in 34 per cent of the cases; of syphilis in 14 per cent, and of diabetes in 10 per cent.

Of the 287 patients studied 117 are known to be living and 142 to have died.

The immediate mortality in the first attack was 16.2 per cent.

Of 117 patients who recovered satisfactorily from the first attack, 75 per cent were in good health at the end of one year; 56 per cent at the end of two years; 21 per cent at five years and 3.4 per cent at ten years. One patient remained in good health for seventeen years and died in a second attack eighteen years after the first.

In 62 per cent of the patients the first attack supervened, without antecedent circulatory symptoms, in persons who had no reason to doubt the integrity of the heart.

A single attack only of thrombosis is recorded in 67 per cent of all the patients; two attacks occurred in 24 per cent; three attacks in 4 per cent and from four to seven attacks in 5 per cent.

Of the patients having but a single attack, one-half are living and one-third are in good health.

Among the patients having two or more attacks the time interval between the first and the second attack was less than one year in half of the cases and in the other half varied from one to eighteen years.

Signs of arterial embolism appeared 49 times among 42 patients. Twenty-eight of the embolic attacks involved the systemic arteries and 21 the pulmonary artery.

Although the immediate mortality in attacks of coronary thrombosis is higher when the initial symptoms are severe than when they are mild, yet almost one-third of the patients who recovered from the attack had symptoms of very severe character.

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# THE EXCITATORY PROCESS OBSERVED IN THE EXPOSED HUMAN HEART*†

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## INTRODUCTION

WHILE the general form of the electrocardiogram is the same for all vertebrates, even closely related mammalian species display curves which differ materially in detail. These differences, which are attributed to variations in the position of the heart with reference to the three standard leads and to peculiarities in the distribution of the ventricular conduction system, have led to considerable uncertainty in the application of the results of animal experiments to the interpretation of clinical electrocardiograms. For this reason studies of the human heart by means of a technique comparable to that employed in animal experiments are of great value. The opportunity to make a study of this kind upon an essentially normal human heart recently presented itself in the person of a young man upon whom a pericardiostomy was performed for suppurative pericarditis complicating a streptococcus pneumonia.

## CASE SUMMARY

A white male, 30 years of age, entered the hospital Feb. 21, 1929, three days after the onset of lobar pneumonia of the lower lobe of the left lung. His past history revealed no symptoms referable to the heart. The physical examination showed the classic signs of pneumonic consolidation of the left lower lobe and revealed the heart to be normal in size and position, regular, rapid and free from any auscultatory signs of pathological change. The roentgenogram taken upon admission (Fig. 1) showed the heart to be normal in size, contour, and position, and also showed the consolidation of the lower lobe of the left lung. Electrocardigrams were usually normal, although at times the T-deflections were inverted in Leads II and III. Culture of the sputum showed streptococcus hemolyticus and streptococcus viridans to be the predominating organisms; pneumococci were not found. On Feb. 28, while the temperature was falling by lysis, a pericardial friction rub appeared and the temperature again rose. An effusion gradually developed and on March 9, a diagnostic puncture of the pericardium yielded sero-purulent fluid containing streptococcus viridans.

On March 12, an extrapleural pericardiostomy was performed under local anesthesia by Dr. John Alexander. The left fifth and sixth costal cartilages were removed, and an opening was made in the pericardium just to the left of the sternum

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from the fourth interspace to the diaphragm, measuring 6 by 4 cm. A considerable portion of the anterior, diaphragmatic and apical surfaces of the heart could be seen through this opening. Fig. 2 is a photograph of the wound made March 21. The opening remained for 21 days; it gradually became smaller so that on March 26, it measured 2.7 by 2.2 cm. The pericardium was irrigated frequently with Dakin's solution and later with 0.1 per cent mercurochrome solution, and the

Fig. 1.—Roentgenogram taken Feb. 21, 1929, showing the heart to be normal in size, contour, and position, and consolidation of the lower lobe of the left lung. The exposure was made with the patient lying on his back and with the tube at a distance of 3 feet.

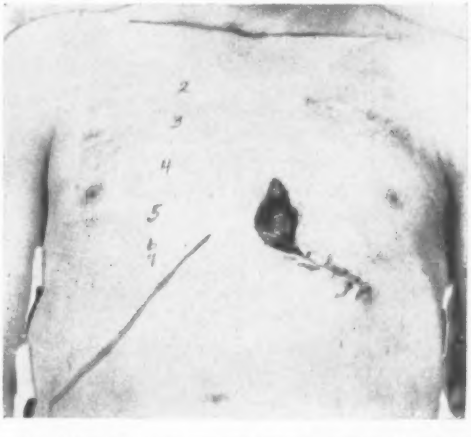


Fig. 2.—Photograph showing the extrapleural pericardiostomy opening through which the heart was studied. The lower anterior surface of the right ventricle and the apex of the left ventricle may be seen. This photograph was made March 21, by which time the opening had become somewhat smaller than when most of the observations were made.

field was kept quite clean. On April 2, the opening was closed under nitrous oxide anesthesia. Up to this time the patient's condition had been good, but bronchopneumonia followed the anesthesia and the patient died on April 3.

The autopsy showed an early disseminated bronchopneumonia, and an older unresolved pneumonia of the left lower lobe. There were two small pockets of

encapsulated empyema, one just to the left of the upper thoracic spine and the other somewhat behind and to the left of the pericardium covering the left ventricle. The heart was normal in size and position and was covered by an organizing fibrinous exudate, but there was no gross abnormality of the musculature, valves, or internal architecture. Microscopically there was subendocardial fatty degenerative infiltration, slight atrophy of the myocardium, cloudy swelling, and early Zenker's necrosis.

The clinical, electrocardiographic, roentgenological, and post-mortem findings indicate, therefore, that for the purpose of the experiments presently to be described the heart was essentially normal in all respects, and that the results of studies made upon it may be applied without reservation to the interpretation of the human electrocardiogram.

When the exposed heart is experimented upon in a human subject only those procedures are justified which can be expeditiously carried out and which entail no great danger or inconvenience to the patient. Two sets of observations which met these requirements and which promised results of value were carried out. The first section of this article is devoted to the normal spread of the excitatory process studied by means of direct electrocardiographic leads from various points upon the ventricles taken simultaneously with standard Lead II. The second section is concerned with the analysis of the curves obtained by electrical stimulation of a series of points on the right and left ventricular surface, and with the bearing of these curves upon the interpretation of clinical electrocardiograms depicting ventricular extrasystoles, bundle-branch block and ventricular preponderance.

## I. THE NORMAL SPREAD OF THE EXCITATORY PROCESS IN THE VENTRICLES

### METHODS—

1. *Electrical Arrangements.*—The method used for studying the order in which various points on the surface of the ventricles became active was essentially that of Lewis and Rothschild[15] in observing this process in the dog. Only their second method in which they employed a single contact on the heart paired with a fixed distal electrode, usually attached to the chest wall, was used in our experiments. It was, however, necessary to make certain modifications of their technique. In the first place, as the heart was not completely exposed it was necessary that the electrode for exploring the ventricular surface be flexible, and since the subject was human, that it be sterilizable.

For this purpose an electrode was devised utilizing the principle described by Adrian[1] whereby a nonpolarizable electrode was obtained by immersing a silver wire coated with electrolytically deposited silver chloride in a solution of sodium chloride. The general construction of this electrode is shown diagrammatically in Fig. 3. This instrument was flexible enough to be bent into whatever shape was necessary, but stiff enough to withstand without bending whatever pressure was necessary to make a satisfactory contact with the ventricle. Sterilization was accomplished by boiling it in strong saline and during the experiment the tip was frequently moistened and cleansed with this solution. The electrode seemed entirely free from polarization effects and though the tip was not so small as that of the instrument used by Lewis and Rothschild, yet, since it was not possible to locate points so accurately as they did, a smaller tip would not have appreciably increased the accuracy of the results so far as nicety of location was concerned.

Since the patient's condition was such that it was deemed unwise to bring him to the laboratory all observations were made over the hospital electrocardiographic distribution system. This limited the number of lead wires with which to obtain two simultaneous records to three. Consequently it was necessary to use the ordinary lead-off from the left leg as the distal contact to be paired with the direct contact and to attach the special electrode to the wire usually employed as lead-off from the left arm. The proper arrangements were then made in the laboratory to obtain ordinary Lead II and the direct lead, special electrode-left leg, simultaneously. The records were taken with two Einthoven galvanometers optically coupled in tandem so that the images of both strings are projected upon the camera in a single homogeneously illuminated optical field. Records were thus obtained whereby it was possible to time the electrical events taking place at that point on the surface of the heart upon which the special electrode had been placed with reference to those of standard Lead II.

2. *Location of points.*—Obviously in an experiment such as this, accurate localization of the points studied was of the utmost importance. To this end an outline drawing of a normal human heart was prepared and the points from which records

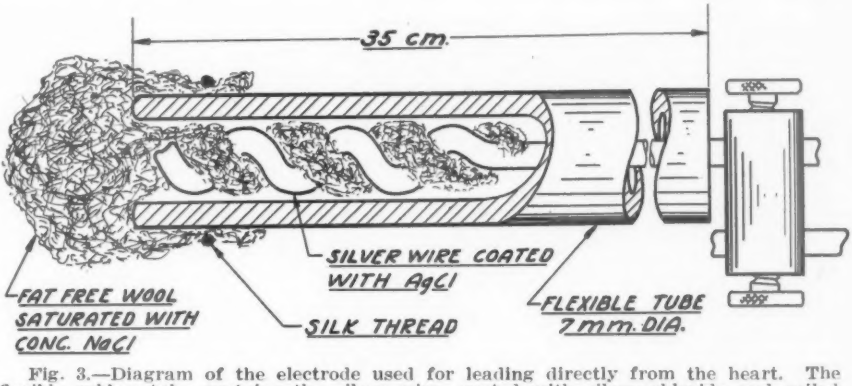


Fig. 3.—Diagram of the electrode used for leading directly from the heart. The flexible rubber tube contains the silver wire, coated with silver chloride and coiled with wool saturated with sodium chloride.

were desired were marked upon it. A few of these points were visible through the wound, *h* and *g* (Fig. 5), *4* and *6* (Fig. 7) and others were just under the edge of the wound *5* and *3* (Fig. 7), *e* and *k* (Fig. 5). The remaining points were located as follows. The surgeon noted the position of these points on the chart with reference to the visible points and with reference to the borders of the heart shown in the outline drawing. He then laid the electrode upon the surface of the chest and measured the distance from the edge of the wound to the surface landmark; rib, interspace, sternal edge as the case might be, which he estimated to lie immediately over the point desired. The electrode was then introduced beneath the edge of the wound for the measured distance and in the proper direction. In each instance the electrode was held steady while the record was being taken. The records were numbered to correspond with the numbers on the chart. This was easily accomplished as the laboratory and the patient's room were in constant telephonic connection during the experiment. Finally, when the heart was obtained at autopsy all notes were consulted and each point located as accurately as possible. It should be mentioned that the anatomical landmarks on the heart itself could be much more easily recognized at the time of the experiment than at the time of autopsy. At the time of the experiments, there was visible on the surface of the heart at the left margin of the wound a strip of edematous fat, which, as was ascertained post-mortem, lay in the interventricular groove. By lifting the tissue at

Fig. 4.—Curves showing a direct lead (upper) and standard Lead II (lower) taken simultaneously. In *A* the direct lead is from the conus arteriosis (Fig. 5, point *a*); the intrinsic deflection begins .0143 sec. after the beginning of R of Lead II. In *B* the direct lead is from the postero-lateral surface of the left ventricle very near the A-V groove (Fig. 5, point *l*). The ventricular intrinsic deflection begins .0229 sec. after the beginning of R of Lead II.

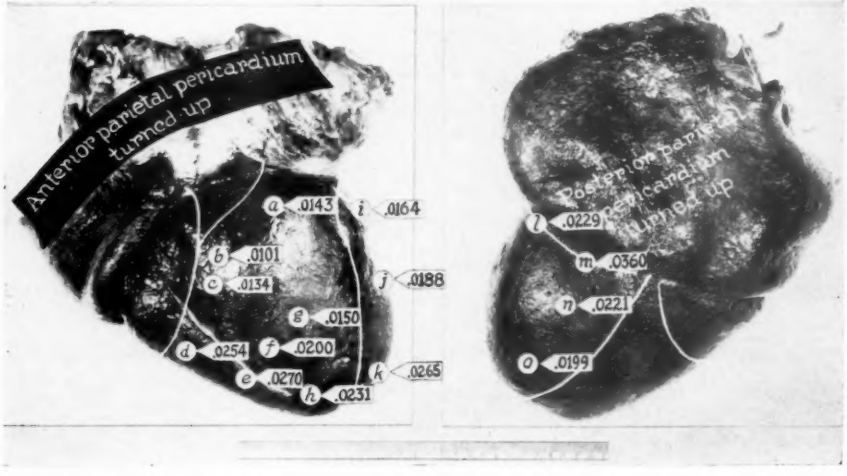


Fig. 5.—Photographs of the heart showing the points from which direct leads were taken and the times after the beginning of R of Lead II at which activity arrived at these points. The white lines mark the interventricular groove, auriculo-ventricular junction, and junction of aorta and conus arteriosus. Points *a*, *i*, and *k* were tested on March 23 and again on March 24, *c* and *f* on March 24, the remaining points on March 23.

the margin of the wound and peering beneath it the apex of the left and a considerable part of the diaphragmatic surface of the right ventricle not directly visible through the wound could be seen.

When the heart was examined post-mortem it was possible to identify the exposed points and those which lay just beneath the margin of the wound with a high degree of accuracy. Regarding the points farthest from the wound, particularly those on the posterior surface of the heart, greater uncertainty exists; but there can be no doubt as to their approximate location.

RESULTS—

All of the curves obtained by direct leads from points on the surface of the ventricles are similar to those described by Lewis and Rothschild.[15] The deflections resemble those of the ordinary electrocardiogram in a general way except that, as a rule, no P-deflections can be made out (Fig. 4). Two elements in the QRS complex are recognizable, a relatively slow deflection, usually directed downward, interrupted by a quick upward deflection of relatively great amplitude, following which the string more slowly returns to the neutral position. This large quick deflection was shown by Lewis and Rothschild to be caused by activity of the muscle directly beneath the electrode and was referred to by them as the intrinsic deflection, all others being called extrinsic. Extrinsic deflections are caused by activity in the muscle elsewhere than beneath the electrode. The intrinsic deflection is recognized by the following characteristics: it is, in any given experiment, always in the same direction (upward in this present one), of large amplitude and short duration; furthermore, the time of its occurrence relative to the beginning of R in Lead II is not altered by changing the position of the distal electrode, even though this procedure greatly modifies the appearance of the complex as a whole. The time after the beginning of R in Lead II at which each of the various points studied on the surface of the ventricle became active was determined, as in the experiment of Lewis and Rothschild, by measuring the time interval from the beginning of the R-wave in Lead II to the beginning of the intrinsic deflection. These time intervals and the locations of the respective points are shown in Fig. 5. The figures represent the average of a number of determinations. The individual measurements varied by less than .001 sec. From a number of points two sets of records were taken, one using the left leg as the distal electrode and one using the right arm. The greatest variation between the times at which the intrinsic deflections occurred in two such records was .002 sec., and in this case the electrode may have moved slightly during the time consumed in making the necessary readjustments for taking the second record. When the same points were studied on different days there was close agreement between the results. As a typical example, the time of arrival of activity at point *a* was on March 23, .0143 sec. and on March 24, .0140 sec. after the beginning of R in Lead II. The Lucas Comparator was used in all cases to measure the records.

The earliest point to become active was *b*, high on the anterior surface of the right ventricle near the tip of the right auricular appendage. This point showed negativity .0101 sec. after the beginning of R in Lead II.

Other early points on the right ventricle were on the conus arteriosus, *a*, and on the anterior surface near the base of the large papillary muscle, *g;* these points became active .0143 and .0150 sec. respectively, after the beginning of R in Lead II. The earliest points on the left ventricle were high on the antero-lateral surface near the left auricular appendage (*i*), and on the left apex posteriorly (*o*); the figures for these points were .0164 and .0199 sec. respectively. The latest point was on the posterior surface of the left ventricle near the atrio-ventricular groove (*m*); it became active .0360 sec. after the beginning of R in Lead II.

## DISCUSSION

The order in which the various points on the surface of the ventricles became active differs in some respects from that found by Lewis and Rothschild[15] in the dog. It will be noted that the earliest points discovered (*b* and *c*) were on the anterior surface of the right ventricle near the atrio-ventricular groove and just inferior to the area where the aorta presents anteriorly. Lewis and Rothschild consistently found the earliest region to become active to be on the anterior surface of the right ventricle near the base of the large papillary muscle, a region corresponding to point *g*, Fig. 5. The difference between their results and ours may be accounted for in a number of ways. It may be the result of a technical error in our experiment. This seems improbable, however, because the readings from points *b* and *c*, which are in close agreement, were obtained on different days, and the results were checked by changing the position of the electrode which was paired with the direct lead. Furthermore, the figures for these points are supported by the early reading from point *a* at the base of the conus arteriosus, which was also checked. This region is relatively late in the dog. It would seem, therefore, that some anatomical explanation for the early arrival of the excitation process at the atrio-ventricular border must be sought. The right atrio-ventricular bundle described by Kent[11] comes to mind, but these results, while consistent with Kent's findings, cannot in the present state of our knowledge be considered evidence for them. Finally, it is possible that the right division of the His-bundle branches earlier than has usually been assumed. No evidence of early branching, or bridging, could be discerned, however, upon gross examination of the heart, and careful study by special methods of the distribution of the conduction tracts was not possible in this case. Differences in the thickness of the ventricular muscle at the points studied cannot be held to account for the

early arrival of excitation at points near the atrio-ventricular groove, because the muscle was thicker at these points than at other relatively early points.

II. THE CURVES PRODUCED BY ELECTRICAL STIMULATION OF THE VENTRICLES

METHODS—

In previous studies of artificially induced extrasystoles in man, mechanical stimulation of the heart has been employed almost exclusively. In the patient studied by the present authors, however neither pricking, pinching nor tapping the ventricles induced premature beats, except infrequently. Electrical stimulation was therefore resorted to. An ordinary Du Bois-Reymond inductorium adjusted to deliver single shocks was used. The secondary was adjusted by trial to deliver stimuli of approximately threshold value, which for most of the regions studied were of about 30 volts.

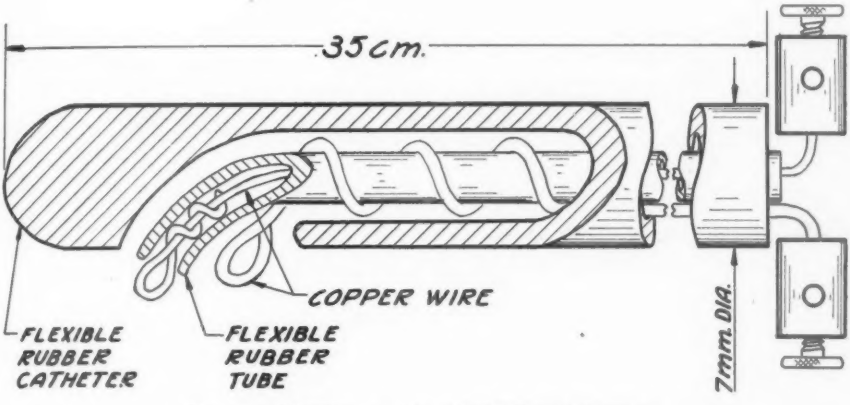


Fig. 6.—Diagram of the stimulating electrode.

As in the case of the non-polarizable electrode already described it was necessary that the stimulating electrode be both flexible and sterilizable. Its general construction is shown in the diagram (Fig. 6). Particular care was taken that the smooth contact points, which were about 3 mm. apart, did not project far beyond the eye of the catheter.

Simultaneous records were obtained according to the method of Einthoven, Bergansius and Bijtel.[4] Lead I was recorded by a large Hindle and Leads II and III by the two Einthoven galvanometers previously referred to. For locating the points stimulated and identifying the records from these points the same method was used as described for the location of points from which direct leads were obtained.

RESULTS—

The electrocardiograms of the premature ventricular contractions induced by electrical stimulation of the ventricles and the locations of the points stimulated are shown in Figs. 7 and 8. These electrocardiograms resemble the clinical records of ventricular extrasystoles. The deflections are essentially diphasic in Leads I and III, in that the T-wave has a direction opposite to the chief initial deflection. The

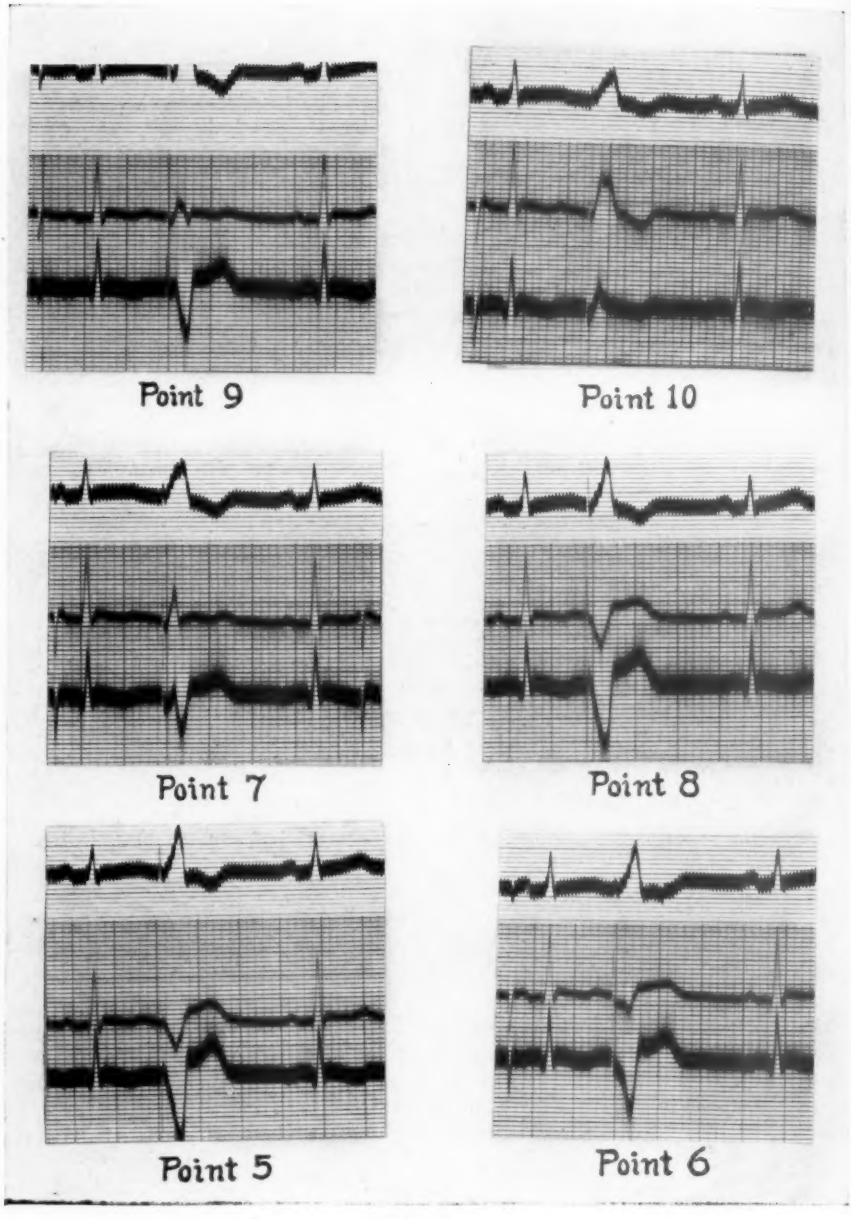


Fig. 7A.

Fig. 7.—Electrocardiograms of the three standard leads taken simultaneously showing the ventricular premature beats induced by direct electrical stimulation of the points indicated on the anterior aspect of the heart on March 19. The forced contractions are preceded by sharp deflections produced by the stimulating current. When the stimulating current fell in the refractory period these sharp deflections are not followed by ventricular complexes. Points *2*, *3*, *4* and *5* were also tested on March 18. Point *1* was tested again on March 24. The top curve is Lead I, the bottom, Lead III.

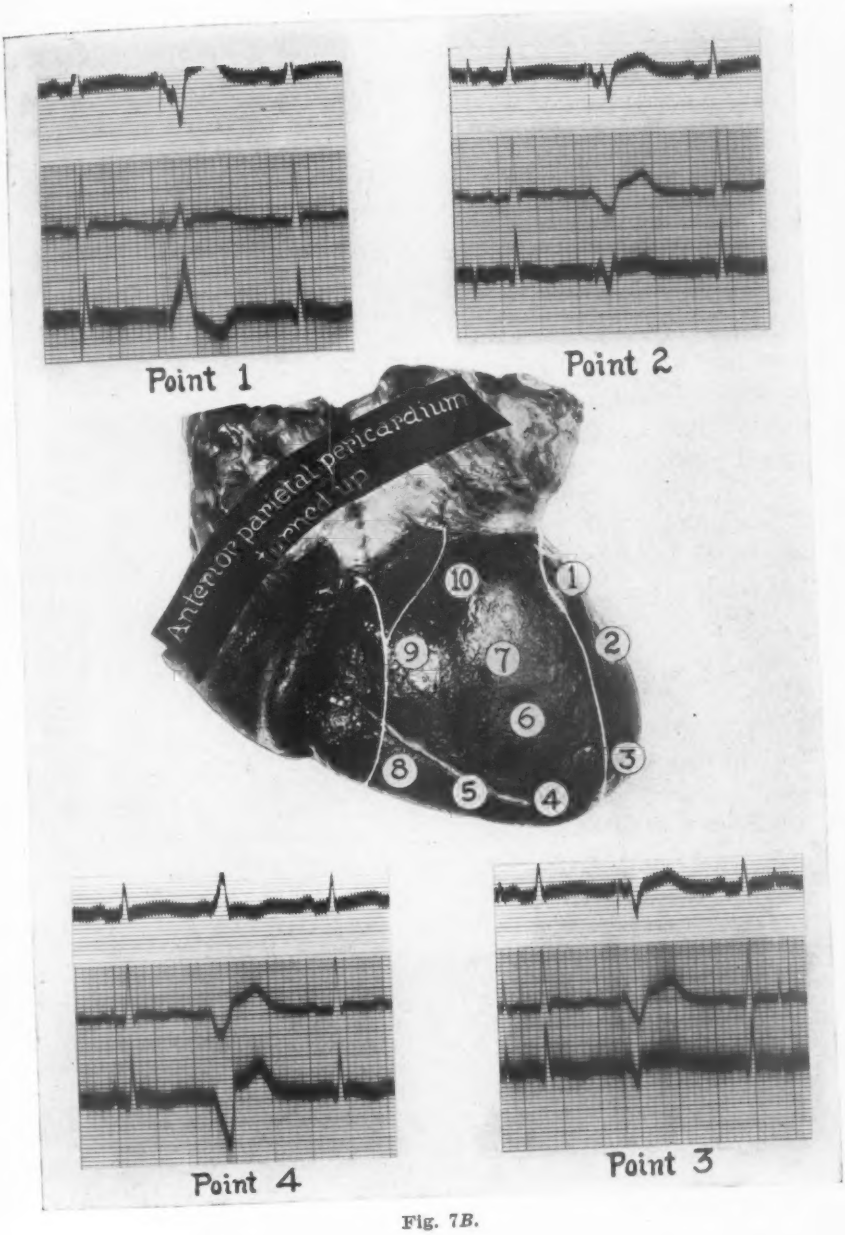
Point 1
Point 2
Anterior parietal pericardium
turned up
10
1
9
7
2
6
3
8
5
4
Point 4
Point 3

Fig. 7B.

QRS interval is much greater than the QRS interval of the normal complexes. These forced contractions may be grouped into four main types: (1) those arising from most of the anterior surface of the right ventricle, which show chief initial deflections that are upward in Lead I and downward in Lead III (points *4, 5, 6, 7, 8, 9);* (2) those arising from the right ventricle in the region of the conus arteriosus, which show chief initial deflections that are upward in all three leads (point *10);* (3) those arising from a point high on the antero-lateral surface of the left ventricle near the left auricular appendage, which show initial deflections that are downward in Lead I and upward in Lead III (point *1);* and (4) those arising from all other points on the surface of the left ventricle, which show chief initial deflections that are downward in all three leads (points *2, 3, 11, 12).* Thus, it is seen that in Lead I all of the chief initial deflections from the right ventricle are upward and all from the left ventricle downward, while in Lead III those arising from the conus and an adjacent area high on the left ventricle are upward and those from all other parts of the heart, including its apical portion, are downward. The deflections in Lead II usually, but by no means always resemble those of Lead III. In Lead II the chief initial deflections are upward in the beats arising from points on the anterior surface of right and left ventricles near the cephalic aspect of the heart and downward in beats arising from all other points.

## DISCUSSION

1. *Ventricular Extrasystoles.*—An experiment such as has just been described might reasonably be expected to answer several questions. First to mind, perhaps, is whether there is any constant characteristic of the curves of premature ventricular contractions which is dependent upon the ventricle from which they arise, or whether the form of such curves is simply determined by the position of their point of origin relative to the base or apex and to the right or left border of the heart quite independently of its relation to the ventricular septum. If points of approximately the same level in the two ventricles are compared (Fig. 7), point *10* with *1*, *7* with *2*, *4* with *3*, it will be seen at once that in all curves from the right ventricle the chief initial deflection is upward in Lead I and in those from the left ventricle it is consistently downward in this lead. That this change in form is attributable to crossing the interventricular septum and not simply to a change in position from right to left can be seen by noting the close similarity between the curves obtained from points *8* and *6* (Fig. 7). These points are much farther apart than any of those previously compared, but are both on the same ventricle at approximately the same distance from the inferior border of the heart. It would seem therefore that when the Purkinje system of the right ventricle is excited in advance of that of the left, an upward deflection occurs in Lead I, and

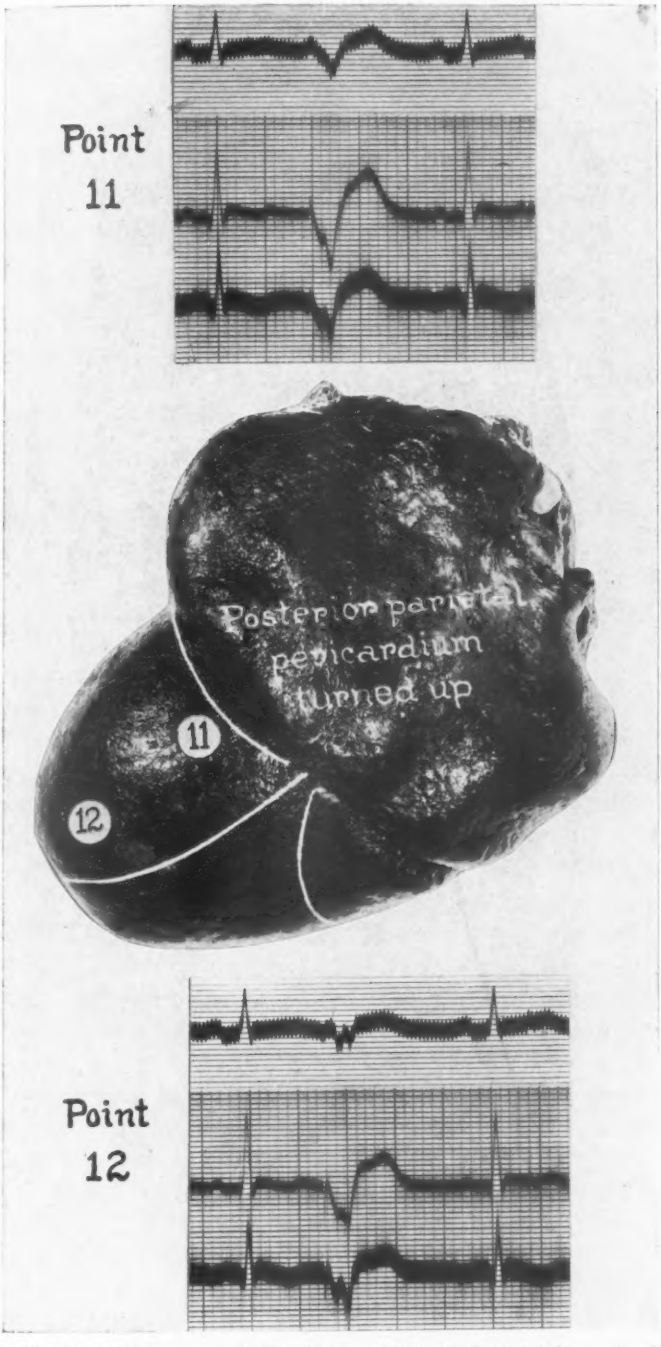


Fig. 8.—Electrocardiograms of the three standard leads taken simultaneously showing the ventricular premature beats induced by direct electrical stimulation of the points indicated on the posterior aspect of the heart on March 19. The top curve is Lead I, the bottom, Lead III.

when the left Purkinje system is excited earlier than the right a downward deflection is produced in this lead.

The position of the point first excited relative to the cephalic and caudal aspects of the heart is, however, not without its effect. As the cephalic aspect of the heart is approached there is a tendency for the chief initial deflection of Leads II and III to become upright, whereas in the more caudal regions this deflection tends to be inverted. On the right ventricle this is best shown in Lead II. If attention be directed to points *10*, *7*, *6*, and *4* (Fig. 7), which are arranged in approximately a straight line from conus to apex, it will be noted that in Lead III the chief initial deflection is upright at point *10* and inverted in all of the other locations, that in Lead II it is upright and of large amplitude at *10*, still upright but of smaller amplitude at *7*, slightly inverted at *6*, and definitely inverted at *4*. This tendency of the chief initial deflection to become more and more inverted as the lower portion of the ventricles is approached is more striking and orderly if reference is made to the cephalic and caudal aspects of the heart as it lies in the body rather than to the apex and base. For example points *8*, *9*, and *10* are all on the basal portion of the right ventricle, but are one above the other with reference to the long axis of the body and it is upon this latter arrangement apparently that the change in the form of the curves obtained from them depends. This change in the form of Leads II and III with the point stimulated is probably caused by the altered order in which various portions of the ventricle become active, or in other words by the altered spread of the impulse through the subendocardial Purkinje plexus, right or left, which it enters first and perhaps to a slight extent by variations in its course through the plexus of the opposite side. This phenomenon is more pronounced in our curves from the right ventricle than in those from the left; the remarkable similarity between the curves obtained from points *2* and *3* leads us to suspect, however, that point *2* was actually closer to point *3* than our chart would indicate. If this is the case the difference between the two ventricles with respect to the phenomenon in question may be more apparent than real.

These observations show that the form of the electrocardiogram of a forced ventricular contraction is dependent not only upon the Purkinje system, right or left, to which the impulse first spreads, but also upon the level with reference to the long axis of the body at which it enters this system. Lead I indicates the former, and leads II and III the latter.

Curves of the type which Lewis[12] has called concordant (main initial ventricular deflections in the same direction in all three leads) and discordant (main deflections not all in the same direction) are obtained from both ventricles. The concordant graphs obtained from the right ventricle (point *10*, Fig. *7*) have upward initial ventricular

deflections and those from the left ventricle, inverted. This is entirely in accord with the accepted view of the subject. The discordant curves, on the other hand, are not in agreement with current electrocardiographic interpretation. In fact, the curves obtained from the right ventricle are of the type which, when naturally occurring, have hitherto been thought to be of left ventricular origin, whereas, the discordant curves obtained from the left ventricle are of the type previously believed to originate in the right ventricle.

The generally accepted view regarding the origin of ventricular extrasystoles represented in the electrocardiogram by curves of the discordant type, with which, as we have pointed out, our results are not in agreement, is derived almost entirely from the current interpretation of clinical electrocardiograms depicting bundle-branch block. As we shall have occasion to discuss this matter in a later section of this article we may omit further consideration of it here.

Our results are similar in a broad sense to those which have been obtained in animals by other investigators. Most of the work on animals, however, was done many years ago and, except in a few instances, only a single lead was employed. For the sake of brevity we shall describe here only the comprehensive investigation of this subject reported by Rothberger and Winterberg[18] in 1913. They employed Lead I and an anus-oesophagus lead. The curves which they obtained from the dog's left ventricle closely resemble those recorded by us from similar locations on the human left ventricle with one exception. They found a small region in the anterior surface of the left ventricle close to the septum which gave discordant curves in which the chief initial deflection was upward in Lead I and downward in the anus-oesophagus lead; no curves of this type were obtained by us from the left ventricle. The curves which they obtained from the dog's right ventricle differ materially from our human curves from this chamber. In their experiments all of the anterior surface of the right ventricle and a narrow basal strip on the posterior surface gave concordant curves in which the chief initial deflection was upright in all leads, whereas in our experiments concordant curves of this type were obtained from a small region on the conus only. From the remainder of the posterior surface of the right ventricle they obtained discordant responses, similar to those which we recorded from the anterior surface of this chamber in man. Rothberger and Winterberg point out at the end of their article that the application of their results to human pathology is not permissible. The wisdom of this reservation is apparent when their curves are compared with those which we have obtained in man, and yet a broad similarity exists.

The present authors were able to find in the literature only four attempts to obtain electrocardiograms of artificially induced extrasystoles in man. The first was that of Hoffmann.[9] His published re-

port, however, does not contain sufficient data to make an evaluation of his results possible. Recently an article appeared by Fossier[7] who induced extrasystoles in a patient who had a congenital deformity of the sternum and in whom the heart was covered by skin and soft tissue only. The heart was stimulated by striking the precordium with a percussion hammer and the three standard leads were taken in rotation. The author interpreted his results as indicating that the form of the forced contractions depended, not upon the ventricle from which they arose, but upon the position of their points of origin relative to the base or apex of the heart. It is probable, however, that the location of the points stimulated was not as accurate as the author believed. It would require only slight reinterpretation of the locations of these points to bring his results into agreement with those here reported.

The most important previous attempt to obtain extrasystoles from known locations on the human ventricles was that of Oppenheimer and Stewart.[17] These investigators studied a patient who had had a resection of all the ribs on the left side excepting the first. The costal cartilages however remained. This left a part of the heart covered solely by the skin. The three standard leads were obtained simultaneously and the heart was stimulated by striking it with a percussion hammer. As the authors interpreted their results they believed them to be in harmony with the generally accepted view. Since the heart was displaced to the right, we suggest however that the approach to the heart in their patient permitted them to reach the left ventricle only, a possibility which they discuss in their article.

If it be admitted that the extrasystoles which Oppenheimer and Stewart obtained resulted from stimulation of various points on the left ventricle, their results are not in conflict with those here reported. Under these circumstances the curves which show downward chief deflections in Lead I and upward deflections in Lead III, which they obtained near the auriculo-ventricular junction, correspond to the curves obtained from point *1* (Fig. 7) in this study, and those in which the initial deflections are downward in all three leads, which they obtained from more apical regions correspond to the curves from points *2* and *3* (Fig. 7) and points *11* and *12* (Fig. 8).

Oppenheimer and Stewart also publish a curve which Prof. Einthoven obtained when he stimulated what he believed to be the right ventricle. His patient had had a portion of the sternum and several ribs removed at an operation subsequent to an accident. Einthoven refers to this experiment and publishes the curve in his Nobel lecture,[3] but gives no further details. The curve is of the type obtained by us from point *1*.

Considering the unavoidable inaccuracy in locating the point stimulated when the heart, covered by the skin and subcutaneous tissues,

is stimulated mechanically by striking the precordium, it is obvious that our results are not in conflict with any previous observations reported in the literature. It is apparent also that the current view regarding the site of origin of extrasystoles represented in clinical electrocardiograms by curves of the discordant type are not based upon satisfactory direct observations in man nor upon direct observations in animals, but upon inference. Admitting that forced contractions produced by electrical stimulation of the epicardial surface of the ventricles are not necessarily comparable in all respects to extrasystoles of spontaneous origin, which are widely held to arise within the special tissues, we suggest that this view should be revised in accordance with the evidence which we have presented.

2. *Bundle-Branch Block.*—The observations which we have described were planned and carried out with the hope of obtaining information bearing upon the interpretation of human branch block and preponderance curves. This hope was founded upon the belief, which is widely expressed and implied in the literature, that the ventricular complexes produced by stimulating the right or left ventricle and those produced by cutting the opposite branch of the His-bundle are similar in form. This belief is derived both from observation and from theoretical considerations.

When one branch of the His-bundle is cut, an impulse which descends from the auricles passes down the intact branch and spreads through the subendocardial Purkinje plexus of the contralateral ventricle and outward through its walls exactly as before. It does not reach the subendocardial plexus of the homolateral ventricle until it has pierced the septum and the activation of this chamber is considerably delayed.

As Lewis[14] and Wilson and Herrmann[20] have pointed out, the course of the excitation wave set up when one ventricle is stimulated electrically is in many respects similar. From the point of stimulation the excitation process spreads in all directions with the slow speed characteristic of conduction in ventricular muscle. As soon as it reaches the subendocardial plexus, however, it spreads with great rapidity over the entire endocardial surface of the ventricle stimulated. The activation of the muscle of the other ventricle is delayed to the same, or nearly the same, extent as in bundle-branch block.

In both cases, therefore, the muscle of one ventricle is activated considerably in advance of the muscle of the other, and in both cases the excitation process spreads with great rapidity over the endocardial surface of this ventricle and traverses its walls from within outward. The course taken by the excitation wave through the subendocardial Purkinje plexus of this ventricle will differ in the two cases, but to what extent will depend upon the location of the point stimulated upon the surface of the heart. If the forced excitation wave enters the

Purkinje plexus in a region that is one of the first to which the natural impulse spreads, the difference will probably be slight; if it enters this plexus in a region which is naturally a late one, the difference may be considerable.

The form of the ventricular complex is determined by the direction and order in which the ventricular muscle passes into the active state, and the considerations outlined above indicate that the ventricular complexes produced by cutting one branch of the His-bundle and those produced by stimulating the opposite ventricle will be similar, but that the degree of similarity will depend to a considerable extent upon the point stimulated.

In describing an experiment in which the effect of stimulating a series of points on the anterior surface of the dog's heart were recorded in Lead II, Lewis[13] called attention to the similarity between the responses obtained from the right and left ventricles and the complexes produced by cutting the opposite bundle in each case. He pointed out that when the usual leads and usual string sensitivity were employed, stimulation of the ventricular surface produced little or no movement of the galvanometer string until the Purkinje plexus was involved. The theoretical considerations, essentially those outlined above, which he puts forward to explain the similarity of the curves obtained by stimulation of a large area of the right or left ventricle apply with equal force to the resemblance between right or left ventricular responses and left or right branch block curves respectively.

Wilson and Herrmann[20] showed that in many instances stimulation of the right central region in the dog produced complexes, not merely similar, but practically identical in the single lead employed, with the complexes obtained by cutting the left branch of the His-bundle. They demonstrated also that when right branch block was present, stimulation of the right central region at the proper instant in late diastole, so that the forced excitation wave reached the terminals of the right branch of the His-bundle at the same instant that the natural impulse reached the terminals of the left branch, resulted in a complex hardly distinguishable from the normal complexes of the same animal. When the right branch block complex and the forced complex were charted and added algebraically in the proper time relations the same result was obtained. They point out that the point stimulated in this instance lay approximately over the point where the right branch of the His-bundle breaks into its arborization. Assuming that this branch gives off no important subdivisions at a higher level, the reason for the similarity between the forced complexes and those obtained by cutting the left branch of the His-bundle are obvious.

Although in the experiments referred to only a single lead was employed the theoretical considerations apply to all three leads with

equal force.* Furthermore the similarity in question is not merely a general one, but often extends, at least in single leads, to the minor details.

On the other hand it is obvious that stimulation of all points on the right or left ventricle does not necessarily give complexes bearing a close resemblance in all leads to those produced by cutting the opposite branch of the His-bundle. In the dog and in man both concordant and discordant curves are obtained from both ventricles. In the dog the chief initial deflection is upright in all leads in left branch block and inverted in all leads, except in rare instances, in right branch block. Stimulation of the anterior surface of the right ventricle, including the region overlying the anterior papillary muscle where the right branch of the His-bundle breaks into its arborization, produces complexes which resemble left branch block complexes in all leads. Stimulation of a considerable portion of the posterior surface produces curves which resemble left branch block curves in Lead I only. Stimulation of the larger part of the surface of the left ventricle also produces curves which resemble those obtained by cutting the opposite branch of the bundle in all leads. There is a small region near the septum at the apex which gives curves which resemble right branch block curves in Lead III only, and another small region at the base which gives responses which resemble right branch block curves in Lead I only. No point on either ventricle gives complexes which resemble those produced by cutting the bundle branch on the same side in all leads, or differ from those produced by cutting the opposite bundle branch in all leads.

When the complexes obtained by stimulation of the human ventricles are examined with these facts and considerations in mind, it will be seen that they are in apparent conflict with the current interpretation of clinical bundle-branch block curves.

The curves obtained by stimulation of the anterior surface of the right ventricle, except a small region on the conus, closely resemble in all leads the curves which are at present ascribed to right branch block. There are three possibilities to be considered.

1). The curves obtained by stimulation of the anterior surface of the right ventricle, including the central region and other points which are naturally activated early, resemble the curves produced by cutting the opposite bundle branch *in all leads*, as they do in the dog.

2). These curves resemble the curves produced by lesions of the bundle branch on the same side *in all leads*, but do not resemble the curves produced by lesions of the opposite bundle branch *in any lead*.

3). The resemblance in question is accidental and without significance.

*With the help of Dr. Wilson we have repeated the experiments which he did with Herrmann, recording Leads I and III simultaneously. The results were identical.

Of these possibilities only the first appears to us acceptable, and we suggest for this reason that the electrocardiograms now regarded as indicating right branch block in man are in reality due to left branch block and *vice versa*.*

In the case of the left ventricle, the conflict between our results and the current view of bundle-branch block in man is less evident. Most of the points on this ventricle gave concordant curves which do not resemble one type of branch block curves more than the other. A single point (point *1*), however, gave curves which resemble those at present ascribed to left branch block in all leads, but do not resemble so-called right branch block curves in any lead. It should be noted that the greater thickness of the left ventricular wall and the fanwise spread of its conduction system make it more difficult than in the case of the right ventricle to so place a stimulus on the epicardial surface that it will spread over the muscle of this chamber in a manner similar to the natural one.

It is now necessary to examine the foundation upon which the current interpretation of bundle-branch block curves in man rests.

The pioneer work in this field was that of Eppinger and Stoerk[5] who studied two patients whose electrocardiograms constantly showed broad diphasic ventricular complexes, the initial deflections of which were upward in Lead I and downward in Lead III. The downward deflections in Lead III were thought to be comparable to the similar deflections which Eppinger and Rothberger obtained from an anus-oesophagus lead in a dog, the right branch of whose His-bundle had been damaged. They therefore diagnosed the condition in these patients as right branch block and at autopsy found lesions involving this branch of the bundle.

This work was confirmed by Lewis[13] in his exhaustive analysis of the electrocardiogram. He first showed that when in a dog either bundle branch was cut the excitation process reached the contralateral ventricle and spread over it in a normal manner, but that it did not reach the homolateral ventricle until later, and that it spread over this ventricle aberrantly. He concluded that the first portion of the initial phases of the abnormal ventricular complexes in right branch block was the graph of the normal spread of activity in the left ventricle, and that the corresponding portion of the left branch-block complexes was the graph of the normal spread of activity in the right ventricle. The former he called the levocardiogram and the latter the dextrocardiogram. In proof of this idea he showed that when the levocardiogram and dextrocardiogram were isochronously summated, the bicardiogram thus produced very closely resembled the normal electrocardiogram.

*This view was advanced some years ago by Fahr[6], as a result of theoretical considerations.

By determining the amplitude of the curves in each of the three leads at many isochronous points he demonstrated that the electrical axis of the heart rotated in a clockwise direction when the left bundle branch had been damaged and in an anticlockwise direction when the right bundle branch was rendered non-conducting. The rotation of the electrical axis shown by the ordinary concordant curves of the dog was much less uniform than that shown by the relatively rare discordant right branch block curves obtained from this animal and by the discordant curves of a large Rhesus monkey. Then with the work of Eppinger and Stoerk in mind he examined human curves of the type which they from their pathological studies believed to be characteristic of right bundle-branch block. He found that these also showed a rotation of the electrical axis in a counter-clockwise direction. He also analyzed a clinical curve of the opposite type, believed to represent left branch block, and found that in this case the electrical axis rotated in a clockwise direction. He pointed out that in dogs the behavior of the electrical axis during the inscription of the dextrocardiogram, or levocardiogram as the case might be, was in harmony with the spread of the excitation wave over the corresponding ventricle. At each instant the electrical axis assumed the direction of the average spread of excitation referred to the plane of the three leads, in so far as this could be determined from his previous studies of ventricular activation.

He concluded that the human levocardiogram was characterized by a diphasic ventricular complex the initial phase of which was upward in Lead I and downward in Lead III and that in the human dextrocardiogram the initial phase was directed downward in Lead I and upward in Lead III. This conclusion rests mainly upon the resemblance between the human curves now ascribed to right branch block, the relatively rare discordant right branch block curves of the dog, and the discordant branch block curves of the single Rhesus monkey examined. Since the electrical axis is derived from the ordinates of the deflection in the three leads a similarity in its direction, or changes in direction from instant to instant, is not more fundamental so it seems to us, than a similarity in the form of the electrocardiogram. Admitting that the resemblance referred to between certain clinical and certain experimental electrocardiograms supports the current interpretation of human branch block curves, it may be pointed out that even within a single species there is considerable variation in the form of the ventricular complexes obtained by cutting the branches of the His-bundle. This is shown by the right branch block curves of the dog which are sometimes discordant, although usually of the concordant type. It is also apparent that not all species of monkeys yield curves of the same kind; in contrast to the discordant curves obtained by Lewis from a *Rhesus* monkey. Wilson and Herrmann[20]

obtained concordant curves from a monkey of the genus *Cercopithecus*. If such differences exist between closely related animals even greater differences between animals and man are not improbable. The heart of man is much larger than that of the experimental animals, and this factor as well as differences in its position and in the distribution of its conduction system may influence the form of the human curves.

Aside from the experimental work of Lewis the studies of Eppinger and Stoerk are the chief evidence upon which the identification of the human levocardiogram rests and the identification of the human dextrocardiogram is largely inferential. Convincing as this classic paper is, there is one point where error might have been introduced. That is, the criteria for believing that the muscle strand which was interrupted by the discovered lesion was the right branch of the His-bundle were not given. This would perhaps seem unnecessary, but as the Purkinje tissue is differentiated only with difficulty from the surrounding muscle in man such evidence is of paramount importance for it is the keystone of the entire structure of the argument. While certain cases have been described in confirmation of the observations of Eppinger and Stoerk,[10] there have been about as many which contradict them[16, 19] and in most instances no lesions of any sort have been found[2] to account for the abnormal curves. Because of the unsatisfactory nature of these pathological studies any definite and well-controlled physiological observations bearing on this subject would seem to be preferable evidence.

The present authors believe that they have presented such physiological evidence in ascertaining the forms of the ventricular premature beats produced by stimulating accurately located points on the surface of the human ventricles. This evidence, as we have pointed out, indicates that the human levocardiogram is a broad notched diphasic curve the principal deflection of which is downward in Lead I and upward in Lead III, and that the human dextrocardiogram is a similar curve in which the main deflection is upward in Lead I and downward in Lead III.

3. *Ventricular Preponderance.*—It has long been known that disorders which tend to produce preponderant hypertrophy of the right ventricle, such as mitral stenosis and certain forms of congenital heart disease, are very frequently associated with electrocardiograms in which the chief initial deflection is downward in Lead I and upward in Lead III; and that disorders which tend to produce preponderant hypertrophy of the left ventricle, such as hypertension and aortic disease, are still more frequently associated with electrocardiograms of the opposite type. In conformity with the current interpretation of bundle-branch block curves it is at present held that the form of the electrocardiograms in question is dependent upon the relatively increased mass of the muscle of the right or left ventricle as the case may be. If what are now regarded

as right ventricular effects in the human electrocardiogram are in reality left ventricular effects and *vice versa*, some other explanation of the form of these curves must be offered which will account for the predominance of the effects of the smaller ventricle. It is possible that this may be brought about by changes in the position of the heart; that is to say, by rotation of the heart about is long axis produced by enlargement of the one or the other ventricle. It seems more probable, however, that it is the result of a defect in the conduction system of the enlarged ventricle which delays the activation of this chamber and permits the smaller ventricle to control the early phases of the ventricular complex. The conduction defect may be the result of mere lengthening of the conducting tracts of the enlarged ventricle, as Fahr[6] has suggested, or more probably of injury of these tissues resulting directly or indirectly from a prolonged increase in intraventricular tension.

Although this explanation of the curves under discussion is not entirely satisfactory, it is perhaps not less so than the one at present accepted. It accounts, for instance, for the serious discrepancies between the form of the electrocardiogram and the relative weights of the two ventricles found in some of the cases studied by Herrmann and Wilson.[8] It also accounts for the observation that $Q$ is largest in Lead I in left and largest in Lead III in right ventricular preponderance. This deflection is the graph of the activation of the first ventricular region to which the excitation wave normally spreads; it is difficult to see how the location or order of activation of this region can depend upon the relative weights of the two ventricles. If, on the other hand, preponderance curves are the result of conduction defects the variations in the form of $Q$ are easily explained since the earliest region to pass into the excited state will lie in the right or left ventricle according to the bundle branch affected. It may be pointed out here that in the electrocardiogram of the new-born infant, $Q$ is largest in Lead III as in other curves which display right ventricular preponderance, which suggests that the form of the infant's curve is not dependent upon the relatively greater weight of the right ventricle, but upon some peculiarity of the conducting system or of the position of the heart.

## SUMMARY

1. A study of the arrival of the excitation process at a number of points on the surface of the human heart with reference to the beginning of R in Lead II was made. It was found that the order of excitation differs in some respects from that found by Lewis and Rothschild in the dog. The earliest points were on the anterior surface of the right ventricle near the atrio-ventricular border. Our results sug-

gest that the conducting tracts in the right ventricle of man may differ from those of the dog.

2. The curves produced by stimulation of various points on the surface of the human heart were recorded in the three standard leads taken simultaneously. These curves indicate that:

(a) Ventricular premature contractions of right ventricular origin are represented in the electrocardiogram by ventricular complexes in which the chief initial deflection is upward in Lead I. Ventricular premature contractions of left ventricular origin are represented in the electrocardiogram by ventricular complexes in which the chief initial deflection is downward in Lead I.

(b) The clinical electrocardiograms at present ascribed to block in the right branch of the His-bundle indicate block in the left branch, and *vice versa*.

(c) In so-called left ventricular preponderance the electrocardiogram is dominated by right ventricular effects and *vice versa*.

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# THE CORONARY ARTERIES OF THE DOG*

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IN THE course of an investigation[1] on the effect of experimental coronary occlusion, it was necessary to study the normal distribution of the coronary arteries in the dog's heart. Our results are somewhat at variance with the generally accepted statement that the coronary arteries of the dog are analagous to those of man. Any comparison of the effects of coronary occlusion in the dog and man must rest on a similar anatomical structure, origin, course and distribution. The literature is reviewed by Spalteholz[2] and need not be given in this paper.

## METHODS

In all, 63 hearts were injected. The injections were made by the technique of Gross.[3] Briefly, this consists of irrigation of the vascular bed with warm water or salt solution (45° C.) and injection of a suspension of barium sulphate in gelatin. After injection, the extraneous injection mass is removed by washing and that in the vessels is hardened by immersion in chilled 10 per cent formalin. Twenty-four hours later, x-ray photographs are taken of the intact and sectioned heart. Routinely, we have taken one radiograph of the intact heart and one of the heart sectioned in such manner that the outer walls of each ventricle are dissociated from the septum. In all photographic reproductions, which accompany this paper, the central portion is the septum, the left portion is the outer wall of the left ventricle and the right portion is the outer wall of the right ventricle. Stereoscopic radiographs were taken of a few hearts. Some hearts were dehydrated and cleared in oil of wintergreen by the technique of Gross.[3]

## THE GENERAL DISTRIBUTION OF THE CORONARY ARTERIES

The coronary arteries of the dog may be divided into four main branches—the right, the left anterior descending, the left circumflex and the left septal arteries. The left coronary arises as one stem in all cases. Within a distance of from 2 to 4 mm. it divides into three branches, septal, circumflex, and descending.

The septal artery, which varies in diameter from 0.5 to 1 mm., passes directly into the muscular portion of the interventricular septum and divides into two branches, an anterior and posterior. (Fig. 1.) From these, there are numerous small twigs which supply the entire central portion of the septum and anastamose with the descending left and circumflex left arteries. A few branches of the posterior ramus ascend to the membranous portion of the septum and supply the main stem of the bundle of His. It is important to note, that the course of this septal

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artery does not appear in the subepicardial fat and hence any experimental interruption of the septal circulation in the dog is extremely difficult.

The anterior descending branch of the left coronary artery, 1.5 to 2.0 mm. in diameter, courses in the subpericardial fat along the anterior interventricular sulcus to the apex of the heart. Three groups of branches are derived from this vessel, those to the septum, those to the right ventricle, and those to the left ventricle.

The septal branches, 12 to 20 in number, arise at right angles from the under surface of the vessel and penetrate the interventricular septum for a distance of 10 to 20 mm., where they establish contact and slight anastamosis with the terminal twigs of the anterior ramus of the left septal artery. The branches to the right ventricle, 4 to 6 in number, arise at right angles from the right side of the vessel and are distributed to the 6 to 8 mm. of the right ventricle nearest the anterior sulcus. The largest of these branches is the first, which supplies approximately one-half of the conus arteriosus and anastomoses freely with the conus branch of the right coronary artery. The branches of the descending left artery to the left ventricle, 3 to 5 in number, arise from the left side of the vessel at a 30° angle and are distributed to the anterior one-third of the outer wall of the left ventricle (Fig. 1).

The circumflex branch of the left coronary artery is the largest, varying from 2 to 3 mm. in diameter. It courses in the auriculo-ventricular groove from its origin to the posterior interventricular sulcus, where it turns toward the apex and forms the posterior descending artery. Four groups of vessels arise from the left circumflex artery; branches to the left ventricle, to the right ventricle, to the septum, and to the auricles. In the auriculo-ventricular sulcus, there arise 6 to 8 right-angle branches which are distributed to the posterior two-thirds of the outer wall of the left ventricle. (Fig. 2.) The first of these is constant and fills the angle between the circumflex and anterior descending left arteries. In 75 per cent of hearts it arises from the circumflex and in 25 per cent from the anterior descending left. From the posterior descending artery, the branches to the septum and to the right ventricle arise in an analagous manner to those of the anterior descending artery. The posterior descending artery usually continues over the apex and supplies the extreme tip of the right ventricle (Figs. 2 and 3). The auricular branches are two in number, a proximal and distal. The proximal artery arises from the upper surface of the circumflex artery, 3 to 7 mm. from its origin and supplies the anterior half of the left auricle, left auricular appendage, and the anterior half of the interauricular septum. The distal artery arises near the posterior interventricular sulcus and supplies the posterior half of the left auricle and a small portion of the central part of the interauricular septum. There are abundant anastamoses between these vessels and the auricular

Fig. 2.

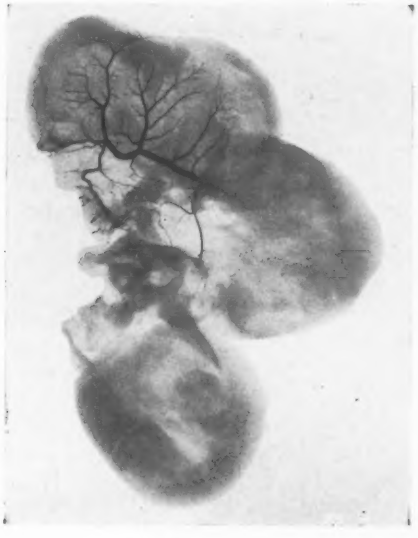

Fig. 4.

Fig. 1.

Fig. 3.

Fig. 1.—Injection of anterior descending left and septal left arteries. Note the branches to the conus arteriosus, the definite central area of the septum supplied by the septal artery and the collateral filling of the circumflex left and right arteries.

Fig. 2.—Injection of circumflex left artery. Note the area at the extreme tip of the right ventricle supplied by this vessel and the collateral filling of all other vessels.

Fig. 3.—Injection of entire left coronary artery.

Fig. 4.—Injection of the right artery. Note the two auricular branches and the abundant anastamoses between them.

branches of the right coronary artery. It is important to note that in 63 hearts, the posterior descending artery was invariably a continuation of the left circumflex artery and never appeared as a continuation of the right artery. Gross[3] states that such a condition is observed in only

Fig. 5.—The region of the auricular arteries posterior to the aorta to show the abundant anastamoses between the right and left proximal auricular arteries.

Fig. 6.

Fig. 7.

Fig. 6.—Experimental ligation of the anterior descending artery to show the filling of the vessel below the ligature through collateral channels. Compare with Fig. 7.

Fig. 7.—Experimental ligation of the anterior descending artery to show complete absence of collateral circulation. Compare with Fig. 6.

20 per cent of human hearts. The entire circulation of the left coronary artery is shown in Fig. 3.

The right coronary artery arises in 80 per cent of cases as a single vessel and in 20 per cent as two vessels. It courses in the auriculoventricular sulcus and gives auricular and ventricular branches (Fig.

4). The ventricular branches are 4 to 8 in number and pass perpendicularly down the surface of the right ventricle. The first branch is constant and is distributed to the conus arteriosus where it anastamoses freely with the conus branches of the anterior descending left artery. In 20 per cent of cases, it arises from the aorta independent of the main artery. The auricular branches are 2 in number, a proximal and distal. The proximal arises 2 to 8 mm. from the aorta and courses through the right auricle and auricular appendage where it anastamoses with the proximal left auricular artery posterior to the aorta. The distal auricular artery arises near the posterior interventricular sulcus and courses toward the mouth of the superior vena cava. In the region of the sino-auricular node it anastamoses with the right proximal auricular and both left auricular arteries (Fig. 5).

### THE BLOOD SUPPLY TO THE SEPARATE PARTS OF THE HEART

In order to render the results more definite, the distribution of the vessels will be rearranged on the basis of the outer wall of the right ventricle, the outer wall of the left ventricle, the septum and the auricles.

The outer wall of the right ventricle is supplied by branches of the left anterior descending, the left posterior descending and the right coronary arteries. The left anterior descending artery supplies the 6 to 8 mm. of the outer right ventricular wall adjacent to the anterior interventricular sulcus (Fig. 1). In the region of the conus this supply is definite and extends over one-half of the entire conus. The posterior left descending artery supplies the extreme apex of the outer right ventricular wall (Fig. 2) and occasionally the 2 to 4 mm. of outer wall adjacent to the posterior interventricular sulcus (Fig. 4). The remainder of the outer wall is supplied by 4 to 8 perpendicular branches of the right artery, the first of which is constant and supplies one-half the outer wall of the conus. Anastamoses are abundant between the conus branch of the right and left anterior descending arteries, the perpendicular branches of the right and the left posterior descending arteries at the apex, and the perpendicular branches of the right artery and the right ventricular branches of the left anterior and posterior descending arteries.

The outer wall of the left ventricle is supplied by the left anterior descending and left circumflex arteries. The former is distributed to the anterior third and the latter to the posterior two-thirds. The angle between the origin of these two vessels is supplied by a branch, which usually arises from the circumflex (75 per cent), but occasionally from the left anterior descending artery (Fig. 3). The degree of anastamosis between these two vessels is variable, but is usually abundant. In Figs. 6 and 7 are two hearts, in which the left anterior descending artery was ligated during life. One hour after ligation the animal was killed and the heart injected. In one (Fig. 6) the anterior descending artery

filled from collateral anastamoses while in the other (Fig. 7) there was no collateral filling. Both were injected at 50 mm. of Hg pressure with all conditions the same. In only three hearts, have we observed complete absence of anastamoses to the left descending artery as shown in Fig. 7. It is possible that injections of the coronary arteries of the beating heart by the method of Wearn[4] would alter this conception of anastamoses. That the filling is not leakage by the ligature is evident from observation of the heart during injection, since the ligated vessel fills from below.

The muscular portion of the interventricular septum derives its blood supply from three sources, the left septal, the left anterior descending and the left posterior descending arteries, all branches of the left coronary artery. The left septal artery supplies the central portion while the septal branches of the two descending arteries send small twigs into the septum for a distance of 6 to 20 mm. The membranous portion of the interventricular septum is supplied in large part by branches of the right and left proximal auricular arteries and in small part by branches of the posterior ramus of the left septal artery. There are abundant anastamoses between these three sources of blood to the septum.

The delineation of definite areas of blood supply in the auricles is impossible because of abundant anastamoses (Fig. 6). The most extensive anastamosis occurs posterior to the aorta between the proximal right and left auricular arteries. The type of anastamosis corresponds to the third variation described by Kugel[5] in the human heart. In no instance have we been able to delineate a definite arteria anastomotica auricularis magna in the dog's heart. In numerous hearts, injection mass in the left coronary artery has been observed to flow across these vessels and fill the main branches of the right coronary artery. (Figs. 1, 2, 3.) No data on the ages of these animals are available and the relation of age to the amount of anastamoses is not known. We have not observed any differences in the hearts from manifestly young animals. In general the auricular branches of the right coronary artery supply the right auricle and those of the left coronary the left auricle.

The sinus node derives its chief supply from the right distal auricular artery but in this region there are abundant anastamoses with the other three auricular arteries. This is in agreement with the findings of Meek, Keenan and Theisen.[6] The auriculo-ventricular node is supplied by the right and left proximal auricular arteries and the bundle of His by the left septal artery.

## SUMMARY

1. The coronary arteries of the dog differ from those of man in two major points: the presence of a distinct and separate septal artery as

a branch of the left coronary artery; and the formation of the posterior descending artery by the left in all cases rather than in 20 per cent as in man.

2. The origin and course of the septal artery renders experimental ligation of it difficult. It is improbable that previous investigators have interrupted the blood supply to the septum.

3. Anastamoses between the coronary arteries and their branches are extremely abundant in the dog's heart.

I wish to thank Dr. L. Katz for the specimens used in this investigation and Dr. H. T. Karsner for aid in the preparation of the manuscript and photographs.

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# VARIATIONS IN HEART-BLOCK SOMETIMES ATTRIBUTED TO A SUPERNORMAL RECOVERY PHASE*

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IN CASES of heart-block a certain peculiar variation has occasionally been observed; auricular beats occurring soon after systole excite the ventricle, while others occurring a little earlier or later in the cycle elicit no ventricular response. Explanations of the variation have logically referred it to those processes which the authors regard as responsible for the block itself. In accordance with the prevailing notion regarding heart-block they attribute this unusual variation to a transient change in A-V "conductivity," even though they are not in agreement regarding the exact causes of such change in conduction. Other authorities, however, have reminded us that the general problem of heart-block is one of too great complexity to permit in every case an interpretation that is concerned only with conduction.

Our case is published because such variations of heart-block are rare, because it shows certain points of difference from the others, and because in it a different explanation of the variation in block (and of the block itself) appears to be indicated.

## CASE REPORT

The patient was a woman fifty-four years of age who entered the Barnes Hospital August 15, 1927, complaining of dyspnea, orthopnea and slow pulse. Dyspnea had begun seven months before admission. Two months later she had consulted a doctor because of an upper respiratory infection. At that time strychnine, iodide and digitalis were ordered. Exact amounts could not be determined, but it was thought that the amount of digitalis was quite small, and the record states that she had had "very little digitalis." There had been giddiness on a few occasions, and in June she experienced a syncopal attack. For the following week she was in bed, and during that period there were several recurrences of syncope. Since that time she had been in bed for the most part and had had no further symptoms.

At examination the patient was in good general condition. There was slight cyanosis of the lips, and the face was somewhat pale. The heart was slow and the impulse vigorous. The rhythm consisted of single and paired beats with a total rate of 45 per minute. There were periods during which only single beats occurred, the rate at such times being 25 per minute. At other times (and this rhythm predominated) the beating was persistently bigeminal. There was a soft murmur accompanying the first sound of the single beats. This systolic murmur was noted also with the first of the bigeminal beats, but not with the second. The blood pressure was 180/50 mm. The Wassermann test was negative. Tests of kidney function gave normal results. The patient remained in the hospital five days, her stay being without important incident. At frequent examinations the heart rate was invariably slow and the rhythm essentially the same as on admission.

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THE ELECTROCARDIOGRAMS

Electrocardiograms were made on August 15, 17, and 20. On August 17, atropine sulphate, gr. $\frac{1}{40}$, was administered intravenously, and records were taken at frequent intervals following the administration. Each record shows a high degree of A-V block, and in each the ventricular rhythm is modified in the manner referred to above. Before discussing the details of this unusual modification of rhythm and its probable import, it will be in order to describe briefly the electrocardiograms that portray it.

The record taken on admission (Fig. 1) shows an auricular rate of 81. There is a high degree of A-V block, only each third auricular impulse producing a ventricular contraction. The conduction time of such auricular impulses as excite the ventricle is not lengthened (P-R, 0.16 sec.). The regular 3:1 sequence, however, is frequently interrupted in the following manner: that auricular beat which occurs immediately after a ventricular systole excites the ventricle again, giving for two successive cycles 1:1 rhythm. Immediately after such bigemini the auricle again fails to excite the ventricle, and 3:1 block supervenes. This interruption of ventricular rhythm, while frequent, is by no means invariable.

The record of August 17 (which is not reproduced) made just before administration of atropine, shows an auricular rate of 100, and for the most part an uninterrupted 3:1 A-V sequence. The P-waves that fall first after ventricular systole are each exactly superimposed on the T-wave, and no bigemini such as are exhibited in Fig. 1 occur. Toward the end of this (long) record, however, the rate of the auricle becomes a little slower and ventricular escape takes place. Under this independent ventricular rhythm, the P- and T-waves are no longer superimposed, and between their peaks appears a space the width of which increases with successive ventricular beats, the T-wave falling earlier and earlier with reference to the P-wave. At a place in the record where this space between T and P becomes comparable to that shown in Fig. 1, the P-wave is followed by a ventricular complex.

It will be noted, then, that this unusual ventricular response occurs, upon occasion, following both types of ventricular systoles; after those consequent upon ventricular escape as well as after those due to effective auricular stimuli in partial heart-block. But in both instances the ventricle responds only to certain ones of the postventricular auricular beats. To which of these auricular stimuli does the ventricle respond, and to which is it silent? What are the conditions limiting ventricular response to particular auricular beats? It was found that those auricular impulses which reach the ventricle during a fixed time interval in its cycle excite it to contraction. This sharply defined interval, measured from the beginning of the R-wave, falls near the end of the T-wave. Other auricular stimuli which begin a little earlier

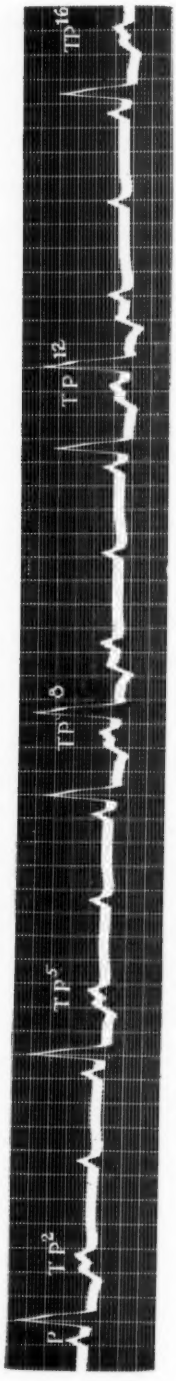


Fig. 1.—Electrocardiogram (Lead II) made August 15, 1927. Discussion in the text.

or a little later elicit no response. *Either they fail to reach the ventricle, or reaching it, they are ineffective.* In order to elicit a response, therefore, an auricular stimulus falling after a ventricular systole, must have its beginning during a certain period following the systole.

Whether or not any of the P-waves in a given record were located within this area of response was found to depend on several factors. (*a*) Consideration had first to be given to the type of *ventricular mechanism.* When complete A-V dissociation (ventricular escape) obtained, P-waves fell at quite different intervals after the beginning of R, and sooner or later an R-P interval occurred whose length was such as to place the P-wave within the area of response. Auricular rate, therefore, was not a factor. (*b*) With 3:1 block, on the other hand, *auricular rate* became a determining factor. For, since the P-R interval remained constant, the auricular rate determined the time interval at which P fell after R, i.e., the R-P interval. (*c*) *Duration of systole* was found to be a factor of crucial importance in both types of ventricular mechanism. It was stated that an auricular impulse, in order to be effective in producing a bigeminal beat, must arise at such a time as would allow it to reach the ventricle in that phase of its cycle corresponding in the electrocardiogram to a certain *critical zone* near the end of the T-wave. Now the duration of systole, as indicated by the duration of the ventricular complex, was longer for idioventricular beats than for beats of supraventricular origin. Since, then, the position of this critical zone, which may be designated "C," or the R-C interval, differed in the two types of systoles, it follows that effective auricular beats occurring after one type of systoles, must of necessity begin (measured from R) at a time interval different from that of the beats which follow the other type. The proposition may be stated in another way: An auricular beat so placed as to excite the ventricle after one type of ventricular systoles, must fall at a different time interval in order to be effective with the other type. It follows that the R-P intervals of effective auricular beats must differ in the two types of mechanism.

Another factor has a well-known influence on the duration of systole, i.e., ventricular rate. Particular reference will presently be made to the influence of ventricular rate upon certain other important features of rhythm displayed by the electrocardiograms. So far as its effect upon the occurrence of bigeminal beats is concerned, it may be said that the rate with 3:1 block differed very little from that following ventricular escape, and that only slight variations in ventricular rate occurred in either type of mechanism. Differences in ventricular rate in a given record had little to do, therefore, with variations in ventricular response. But the basic rate of the ventricle at a given time was an important factor in determining whether or not definitely placed auricular beats could elicit a response.

The net result of the above factors may be quite simply stated: Whether or not a given auricular beat occurring soon after ventricular systole is found to excite the ventricle, depends upon the relation of the R-P interval to the R-C interval. Now, it has just been shown that the R-C interval depends upon the R-T interval. It follows, therefore, that ventricular response is determined by the relationship of R-P to R-T. But since with 3:1 block, R-P is determined by the auricular rate, and since R-T depends upon the rate of the ventricle, it follows further, that the matter of ventricular response is determined (1) in 3:1 block by the relationship between auricular rate and ventricular rate; (2) with ventricular escape, by the chance position of the P-wave in the ventricular cycle. It may be stated further that, in the case of 3:1 block, variations in the R-P:R-T ratio in a given record, are due almost entirely to *variations in auricular rate*, differences in the R-T intervals, as above noted, being of slight extent because of the relatively slight changes in ventricular rate.*

The above statements receive abundant confirmation in the records. Fig. 2 is a record in Lead III made during a forced respiration. It shows an arrhythmia of the auricles to which attention has frequently been called in reports of heart-block. That interauricular interval which includes ventricular systole is shortened. But these intervals themselves show a variation that is a part of a general change in auricular rate with respiration. At the right end of the record the rate is essentially the same at the beginning. Between these portions it becomes slower and then faster. With the slowing, the R-P interval increases and thus the P-wave is placed too late for its impulse to reach the ventricle during C. With acceleration the R-P interval shortens until P falls early enough to reach the ventricle before the termination of C. These observations are verified not only by measurements of corresponding auricular cycles but also by mere inspection of the successive T-P intervals.

Similar tests applied to Fig. 3 demonstrate the same facts. The sixth interauricular interval is longer than the third. Auricular rate was becoming slower, and that the retardation was continued is shown by the fact that the seventh interval is somewhat longer than the fourth. This is indicated also by the longer T-P interval in the seventh cycle. Auricular rate then became faster, and the tenth P-P interval was short enough for the P-wave to fall within the critical zone C. Fig. 3 illustrates also the later position of C with escaped beats. Although the P-wave, following the escaped beat near the right end of the illustration, falls at a time later after the (projected) beginning of

*It should be borne in mind that this statement regarding ventricular rate refers only to the question so far discussed, i.e., the production of bigemini. Only the interval between a preceding ventricular beat and the *first* beat of the bigemini can be used in considering the question. The R-R interval between the beats of the bigemini themselves represents a much faster rate and is important in another matter which will presently receive consideration.

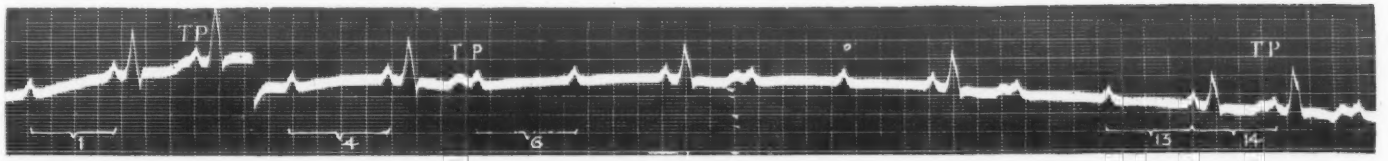


Fig. 2.—Electrocardiogram (Lead III) made August 15, 1927. The brackets 1, 4, 6, etc., indicate corresponding P-P intervals. The auricular rate becomes slower in the midpart of the illustration, and then becomes faster again (respiratory). Note the short T-P intervals with the faster rate at the beginning and at the end of the illustration where the bigemini occur.

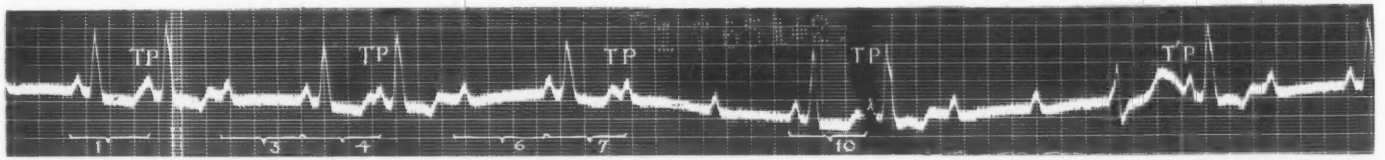


Fig. 3.—Electrocardiogram made August 17, 1927 (six and one-half minutes after the administration of atropine, Lead II). Average auricular rate 85. Note the different lengths of the T-P intervals and the failure of the ventricular response with the long interval above bracket 7. Near the right end of the illustration ventricular escape occurs. With this "escaped" beat the R-P interval requisite for ventricular response is different from that of the other type of systoles.

R than does the P-wave closing the seventh interauricular interval, it is, nevertheless, early enough to excite the ventricle, while the other falls too late to do so. In the light of Figs. 2 and 3, the interpretation of Fig. 1 becomes obvious. With an auricular rate of 82, the postventricular P-waves are falling at such times after R that the impulses reach the ventricle near the termination of C. Impulses from $P_8$ and $P_{12}$ fall just within, those from $P_2$, $P_5$, and $P_{16}$ just without its confines.

Just as a slow auricular rate (long R-P interval) may cause the auricular beat to fall too late to excite the ventricle, so with a faster rate of the auricle its impulse may occur too early (short R-P interval). Such a situation is shown in Fig. 4. The auricular rate in this illustration averages about 95 as compared to an average rate of 85 in Fig. 3. The rates at the extremes of Fig. 4 are identical. There is slight acceleration in the first third of the record, however, the maximum rate being attained about the sixth and seventh interauricular intervals, after which point the rate becomes slower. (Compare interval 5 with 1, 8 and 15; also interval 6 with 2, 9 and 16.) With the acceleration the P-wave closing the sixth interval falls too early and does not excite the ventricle, the rate at that moment being about 100.

Brief consideration should be given to the mechanism responsible for limiting ventricular response to only one auricular stimulus. In the records so far exhibited the P-wave following the second beat of the pair does not again excite the ventricle and thus continue 1:1 rhythm, because of the following facts: (1) The auricular rate, having shown temporary acceleration in the manner that has been described in heart-block and to which reference was made above, becomes slower again. This alone might on occasion be sufficient to terminate the 1:1 rhythm. (2) Another factor, however, operates toward the same result. With the occurrence of the bigeminal beat, the rate of the ventricle is abruptly accelerated to about three times its original level, and the R-T interval of the second beat, therefore, is materially shortened. As a consequence of these changes in ratio of R-P to R-T, the impulse from the P-wave which follows the bigemini falls beyond the critical zone.

*A. Duration of the Critical Zone.*—Consideration has just been given to the interplay of factors responsible for placing the P-wave so that the impulse falls within or without the critical zone C, and to those factors which change the location of this zone itself. Whether or not the stimulus of a given P-wave falls within the confines of this zone, obviously must depend upon the duration, or the width, of the zone. If the width were of sufficient extent, all the P-waves in question would be effective, only 1:1 response would obtain, and there would be no block. It is, in fact, because of its very limitations that cases such as ours come under observation to present a special problem in heart-block.

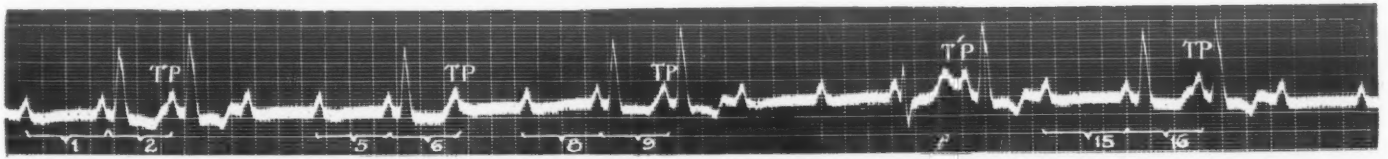


Fig. 4.—Eleven minutes after atropine (Lead II). Average auricular rate 95. Bigeminal beating occurs consistently except after the P-wave which closes the sixth P-P interval. Auricular rate is fastest at that point, and the P-wave falls too early to be effective.

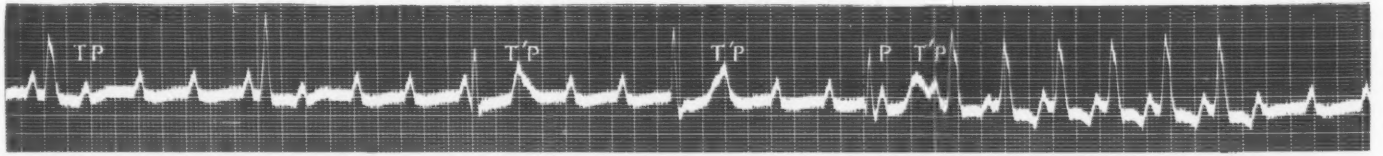


Fig. 5.—Seventeen and one-half minutes after atropine (Lead II). Auricular rate 132. Note that the continued 1:1 rhythm at the right of the illustration is initiated with the second P-wave following an escaped beat. Discussion in the text.

Exact determination of the confines of this zone, with either type of ventricular beats, is difficult, but its approximate location can be fixed. In the case of those beats of supraventricular origin it is arrived at as follows: In Fig. 1, where the P-waves were placed so that their stimuli were reaching the ventricle near the end of C, the longest interval between the beats of the bigemini is 0.7 of a second. P-waves placed even a little later, elicited no ventricular response. Under the conditions of that record, therefore, C ended at about 0.7 of a second after the beginning of R. In Fig. 3 the longest interval (that between the third pair) is about 0.64 of a second after the beginning of R. The ventricular rate in the latter case is somewhat faster than in the former, and this, as above noted, placed C a little earlier. In Fig. 4, on the other hand, the stimuli from auricular beats are falling near the beginning of C. The shortest R-R interval of bigeminal beats (that of the second pair) is 0.59 of a second. An auricular stimulus which arises earlier, reaches the ventricle before the onset of C. Under the conditions recorded in Fig. 4, therefore, the beginning of C is about 0.59 of a second after the beginning of R. It may be stated, then, that with a ventricular rate of 33 per minute (Fig. 4), C begins about 0.59 of a second after the onset of R. With a rate of 30 per minute (Fig. 3), it ends about 0.64 of a second after R, and with a rate of 27 (Fig. 1), it ends about 0.70 of a second after R. From these determinations it would appear that its endpoint is doubtless still earlier with a rate of 33 than with the slower rates, and since its end point with a rate of 30 is 0.64 of a second after R, it probably ends earlier than that with a rate of 33. Now its beginning with the latter rate is 0.59 of a second after R. Its duration, therefore, at a rate of 33 per minute is probably less than 0.05 of a second.

Knowledge of the duration of C may be important from two viewpoints. First, it may be of value in trying to determine the nature of the process responsible for this removal of block over such a brief time interval. Second, it fixes the condition under which 1:1 rhythm may be continued over more than two cycles.

*B. Continued One-to-One Response: Conditions Requisite for Its Inception and Continuation.*—Fig. 5 is a portion of the record made seventeen and one-half minutes after the administration of atropine. The auricular rate is 132. The record contains both types of ventricular complexes, and the zone C, therefore, is located at different intervals in the ventricular cycle. The first ventricular complex is of supraventricular form, and the P-wave that follows it occurs too early for its impulse to reach C.* Ventricular escape takes place, the postventricular P-wave falling later and later with reference to R. But with these "escaped" beats C occupies a later time interval, and even

*With the same ventricular rate in Fig. 4, it was seen that C begins at about 0.59 of a second after the beginning of R.

though the P-waves fall later than did the one first recorded, they are still too early for the auricular stimuli to reach C. Following the fifth ventricular complex, however, the second auricular beat falls at the proper time and a ventricular systole results. But with the occurrence of this systole ventricular rate has become much faster, and the next auricular impulse, though falling at an interval after R which is essentially the same as that recorded at the beginning of the figure, is not now too early to reach C, because the latter, with the faster ventricular rate, has moved forward in the cycle. It is now early enough to catch the auricular impulse, and another ventricular response, therefore, takes place. With this beat *the short R-T interval is continued.* Now the rate of the auricle also is faster than that recorded in any of the previous records, and this produces a short R-P interval; the resulting R-P to R-T ratio being such as to maintain the 1:1 response. The duration of C, its "width," however, is limited, and the auricular stimuli are doubtless falling near the edge of a narrow zone. After a few beats an auricular impulse, because of slight disturbance of the R-P to R-T ratio, falls outside its confines and fails to excite the ventricle.

This figure 5 is a part of a long record showing the same succession of events many times repeated. One-to-one rhythm was invariably initiated in the same manner. It appears, indeed, that it is only in this way, i.e., following an escaped beat with a (second) P-wave falling well on the down slope of T, and at the same time a fast auricular rate, that it is possible for sustained 1:1 rhythm to be initiated. For with an auricular rate fast enough to maintain it in the presence of the (resulting) rapid ventricular rate, it cannot be initiated following a systole that originates in 3:1 block. The ventricular rate in such a case, as noted above, is relatively very slow, and the zone C of such a systole, therefore, is too late for the auricular impulse of such a rapidly beating auricle (and consequent short R-P interval) to reach it. One-to-one rhythm having been initiated, however, in the manner described, the length of R-T is then brought into the proper ratio to R-P, and 1:1 response continues.

It will be observed, then, that both of the unusual modifications of ventricular rhythm recorded in this case, bigeminal beating and continued 1:1 response, are referable to the relationship of the R-P interval to the R-T interval. The effect of atropine in removing the block appears to result only from the acceleration of auricular rate produced by it, and to depend in nowise upon any effect on A-V conduction.

## COMMENT

The removal of block in this case occurs under two circumstances: (1) at the end of a long period, in a manner common to partial heart-

block and calling for no special comment, (2) over a brief span of ventricular systole, before the termination of the above-mentioned period. It is this unusual feature which has sometimes been regarded as resulting from an overswing in the recovery of the A-V tissues and for which, in the present case, a different explanation appears to be indicated.

Two aspects of the problem must be considered: (1) the site at which the removal of block is effected, and (2) the nature of the process effective for so brief an interval at that site. All authors who have reported such cases regard the A-V tissues as the site in question, only Lewis and Master[1] considering the possibility of any other location. There is not such agreement, however, with regard to the second aspect of the problem. Lewis and Master regard the cause as a "supernormal" recovery phase. Ashman and Herrmann,[2] although mentioning possible causes of improvement in conductivity other than an overswing in the recovery curve, favor the same explanation. Wolferth[3] agrees that such a supernormal phase might explain the phenomenon, but he offers alternative explanations to account for the temporary improvement in A-V conductivity.

Whatever the cause of the block recorded in our case, wherever its site, it appears that there is little ground for assuming that its transient removal results from an overswing in the recovery curve of A-V conductivity in the sense that the term was employed by Adrian and Keith Lucas.[4] They found that frog's nerve when bathed in fluid that was relatively acid, showed, during its recovery after excitation, an overswing in the curve of recovery, a "supernormal" phase. They found the same overswing, under like conditions, in the recovery curve of frog's heart muscle after contraction. The records of our case indicate clearly that the relief of block resulted from some effect of the preceding ventricular systole. Its constant position in the ventricular cycle, its different time relationship with systoles of different lengths, admit of no other interpretation. But the records do not imply that the site of this effect is in the A-V tissues. Systole might conceivably produce an overswing of conductivity in the A-V tissues either directly or indirectly. A retrograde impulse sent into the bundle by a ventricular contraction might directly effect such a result. The A-V tissues in their recovery from the conduction of such an impulse might exhibit a supernormal phase. Ashman and Herrmann, indeed, employed this conception in their Case 1 in which the relief of block occurred after an idiopathic ventricular systole from which presumably an impulse might have been sent in retrograde fashion into the bundle. But our case exhibited the phenomenon during partial (3:1) block. The impulse entered the bundle from above, and not as a result of ventricular contraction. Since the systole was of supraventricular origin, therefore, any effect upon the A-V tissues induced by it must have been

an indirect effect. Whether some such indirect effect of ventricular contraction might change the A-V tissues so as to produce exactly the conditions necessary for an overswing in the recovery curve, an overswing, furthermore, which must exactly coincide with the time of the oncoming auricular stimulus, at present would appear to be problematical. No explanation of such a process is proposed by Lewis and Master. It is possible, of course, that systole might temporarily heighten A-V conductivity in some way other than by producing a "supernormal" recovery, a solution of the problem favored by Wolferth.

Neither the precise effect of ventricular contraction that is responsible for the removal of block for so brief an instant, nor the exact site of its application, can be determined merely by a study of clinical records, nor can the cause of the antecedent block. It appears unnecessary to employ various assumptions referring it to the A-V tissues. The simplest explanation would refer it to the ventricle itself, provided such an explanation be in accordance with accepted notions about heart-block.

The theory of heart-block proposed many years ago by Erlanger[5] takes into account not only different degrees of A-V conductivity but also different levels of ventricular irritability (or excitability) and different strengths of auricular stimuli as well. It presupposes that certain auricular impulses may pass the A-V conducting system and still find the ventricle unresponsive. This conception, indeed, is entertained by authorities who, at the same time, are inclined to refer all instances of heart-block to "defective conductivity" alone. They, in common with others, explain the failure of an auricular impulse which, if conducted normally, would reach the ventricle during its refractory phase (following a spontaneous ventricular systole), not as depending upon a temporary defect in the A-V tissues, but as due to a temporary change in ventricular excitability. The block in the present case, indeed, may as well be the result of lowered excitability of the ventricle as of lowered conductivity of the A-V tissues. With this in mind we are prepared to accept the obvious implication of the records which appear to refer variations in the block to variations in ventricular excitability. By the application of Erlanger's theory the phenomena recorded in our case are explained as follows: Due to a lesion in the A-V tissues, which reduces the strength of auricular impulses, or to a condition of lowered excitability in the ventricular muscle, the auricular stimuli arriving at the ventricle are below threshold. After a long recovery period ventricular excitability rises to such a level that the next auricular stimulus is effective (3:1 block). The resulting systole, in some way, causes the curve of ventricular excitability to rise sharply for a brief instant, after which it falls and resumes its gradual rise. If an auricular stimulus happens to arrive

at the ventricle at the moment when excitability is high, another contraction is effected. This second systole produces another brief rise in ventricular excitability which may or may not coincide with the arrival of an auricular impulse—depending on the ratio of R-P to R-T, as already discussed.

As to the process responsible for this transient rise in ventricular excitability, we offer no surmise. An overswing in the recovery curve of ventricular excitability (a possibility suggested by Lewis and Master), if indeed such a phenomenon occurs in mammalian heart muscle, would occupy a phase in the ventricular cycle corresponding essentially to that of the critical zone C during which auricular stimuli are effective. Its location, when observed, is near the end of the refractory period. Its position in the ventricular cycle, therefore, while constant for systoles of the same length, would show with systoles of different lengths correspondingly different intervals after the beginning of R—a characteristic feature of our records and one which it would be difficult to correlate with A-V conductivity.

It is possible that some circulatory or other effect of systole, at present unknown, may occupy only such a phase in the ventricular cycle. Just how systole produces in certain cases of heart-block the auricular arrhythmia referred to is a conspicuous example of some such influence at present not understood. If the cause of the block was indeed a depression of ventricular excitability, then it may be that systole effected an improvement in the physiological properties of the ventricular muscle which, for a brief period, raised ventricular excitability. Until more is known of the effects of systole on various cardiac properties a solution of the problem cannot be reached.

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# THE ADRENALIN TEST IN HYPERTENSION*

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## INTRODUCTION

IN 1894, Oliver and Schafer,[1] and independently of them, Szymonovicz and Cybulski[2] demonstrated that adrenalin had a marked pressor effect on the cardiovascular system. In 1909 Eppinger and Hess[3] used adrenalin as a pharmaco-dynamic test for the symptom complexes which they called sympathicotonia and vagotonia. It was not until three years later, however, that Bauer[4] wrote his fundamental paper on the adrenalin test, and by giving adrenalin subcutaneously, established the character of the reaction of normal individuals. He emphasized the dissociation of the adrenalin effects and the peripheral vasodilatation, and concluded that though patients may have varying vegetative tonus, the use of the drug as a method of differentiating between sympathicotonia and vagotonia was not justified.

The adrenalin test has been used in many clinical conditions and occasionally as a method of differential diagnosis. Goetsch[5] employed it to aid in the recognition of hyperthyroidism but was criticized by Sandiford,[6] Peabody[7] and others. In the clinical states of vascular hypertension the results have been variable. Kylin[8] was the first to call attention to the inconspicuous response met with in cases of hypertension when 1 c.c. of adrenalin is injected subcutaneously. In this finding he varied from Clough[9] who had found exactly the opposite response. Brems[10] and many other authors agreed with Kylin; to these, references may be found in his papers.

Sanguinetti[11] and, independently of him, Csepai[12] believed that by administering adrenalin subcutaneously the factor of difference of absorption is added. They suggested intravenous administration of a much smaller dose. The blood pressure response of the patient with hypertension to this changed technic soon gave rise to another argument. One group, led by Hetenyi and Sümegi[13] and Csepai[12, 14] found universally in hypertension an increase in the adrenalin response, while Deicke and Hülse[15] and others asserted that this increased response was only present when renal damage had occurred.

At present there is no unanimity of opinion concerning the question. This study, therefore, was undertaken for the purpose of determining whether the hypertensive response differs in any characteristic manner from the normal response, and if it does, whether this reaction throws any light upon hypertension. At first an attempt was made to deter-

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mine whether the blood pressure response to adrenalin would be consistent when the test was repeated in the same individual. It was soon found that there were variations so striking as to warrant special study. These have been investigated both in patients with hypertension and in normal individuals.

## PROCEDURE AND MATERIAL

Forty-three persons were selected for adrenalin tests. These were performed before breakfast with the patient still in bed. Some ambulatory patients in whom these conditions were not obtainable rested for twenty to thirty minutes before the test. The cuff was always placed on the right upper arm and the same mercury manometer was used throughout the experiments on the same person. The systole was determined as the highest level where all the beats were plainly audible, and the diastole was the level where the clear sound changed to a muffle. If no such transition was marked, the diastole was taken as the lowest level where the sounds were distinctly heard. The difficulty of this determination did introduce a personal factor into the diastolic readings. Readings were taken every three minutes until a sufficient number were obtained to form some opinion as to the level and variability of the blood pressure. Then 1 c.c. of saline solution was usually injected subcutaneously into the left deltoid region, and readings were continued while the reaction produced by the prick of the needle was observed, usually for nine or ten minutes. Then 1 c.c. of clear colorless adrenalin was injected into the left deltoid region and the site of the injection was thoroughly massaged for thirty seconds. Occasionally the dose was one-half c.c. Thereafter frequent blood pressure and pulse readings were taken, until the reactions immediately following the injection had subsided. Usually blood pressure and pulse readings were taken every three minutes for ninety minutes after the injection of adrenalin. During the early part of the work the pulse was not counted. Occasionally the observation lasted more or less than ninety minutes. Omitting the saline injection the test was then repeated one to four times. All tests were done by me, personally, but most routine blood pressures were taken by the clinical staff. The subcutaneous method was used because it seemed the simplest and because the effects were so protracted that they could be studied in detail. In my opinion absorption did not vary sufficiently to influence the test.

The patients were arranged in the following groups: (1) normal controls, that is, persons with normal cardiovascular systems; (2) patients with pronounced hypertension; (3) patients with early or intermittent hypertension; (4) finally a small group with miscellaneous conditions in which we thought our findings might throw some light upon the manifestations in the patients with hypertension. Included in this group were cases of nephritis, hyperthyroidism, and enlargement of the heart without hypertension. Some of the subjects in groups 1 and 3 were members of the University Hospital Staff.

## RESULTS

A. *The Normal Response to Adrenalin.*—When adrenalin was injected into thirteen normal persons, there followed a higher systolic blood pressure, a lower diastolic pressure, and a more rapid pulse rate. The increase in systolic pressure varied from 15 to 58 mm. Hg, the maximal pressure being reached in from 11 to 46 minutes. The immediate response varied from 8 mm. in 22 minutes to 38 mm. in three and a half minutes. In three cases the pressure increased suddenly.

The decrease in the diastolic pressure amounted to from 8 to 38 mm. Hg and occurred in 5 to 39 minutes and as a rule the pressure returned to normal in 60 to 90 minutes. The pressure usually fell rapidly and returned slowly to normal, but some irregularities occurred, possibly because of errors in reading.

TABLE I

THE INCREASE OF SYSTOLIC BLOOD PRESSURE AFTER 1 C.C. OF ADRENALIN IN TWELVE NORMAL INDIVIDUALS

| PATIENT NO. | TIME OF OBSERVATION (IN MINUTES AFTER INJECTION OF ADRENALIN) | EXTENT OF INCREASE | |
|---|---|---|---|
| | | FIRST TEST | REPEATED TESTS |
| 18 | 7 | 20 | 2 |
| 19 | 4 | 6 | 12 |
| 20 | 8½ | 14 | 54 |
| 21 | 4 | 0 | 26 |
| 22 | 3½ | 38 | 60 |
| 23 | 1 | 0 | 44 |
| 24 | 4 | 4 | 36 |
| 25 | 7 | 12 | 20 |
| 26 | 4 | −4 | 16 |
| 27 | 3 | 30 | 66 |
| 28 | 7 | 30 | 36 |
| 29 | 1 | 2 | 36 |

TABLE II

THE DECREASE OF DIASTOLIC BLOOD PRESSURE AFTER 1 C.C. OF ADRENALIN IN TWELVE NORMAL INDIVIDUALS, THE TIME WHEN THIS DECREASE OCCURRED AND THE TIME CONSUMED ON THE RETURN OF THE PRESSURE TO NORMAL

| CASE NO. | MAXIMUM DECREASE (MM. HG) | TIME OF MAXIMUM DECREASE (MINUTES) | TIME OF RETURN |
|---|---|---|---|
| 18 | 38 | 23 | 86 |
| 19 | 10 | 5 | 45 |
| 20 | 26 | 7 | 67 |
| 21 | 20 | 14 | 56 |
| 22 | ? | ? | — |
| 23 | 20 | 39 | 96 |
| 24 | 8 | 6 | 9 |
| 25 | 14 | 10 | 71 |
| 26 | 24 | 37 | 106 |
| 27 | 26 | 27 | 78 |
| 28 | 20 | 30 | 60 |
| 29 | 18 | 17 | 72 |

The increase in heart rate came in some cases before the systolic rise, in other cases later. It bore no relation to the blood pressure changes. In the few cases which were examined for this point, the increase lasted longer than the changes of either the systolic or the diastolic pressures.

When the tests were repeated in the same individual, the systolic changes remained of the same general character, but in eleven of the twelve cases where the test was repeated in 48 hours or later, the response changed qualitatively, becoming more sudden and more intense.

The findings in Case 18 may be due to delayed absorption, for when the blood pressure finally increased it rose more sharply than on the first occasion. In cases 25, 27, and 30, a second injection was given in three hours or less. The rise was slower, less extensive and poorly sustained. The nature of this change in response was not clear. Pos-

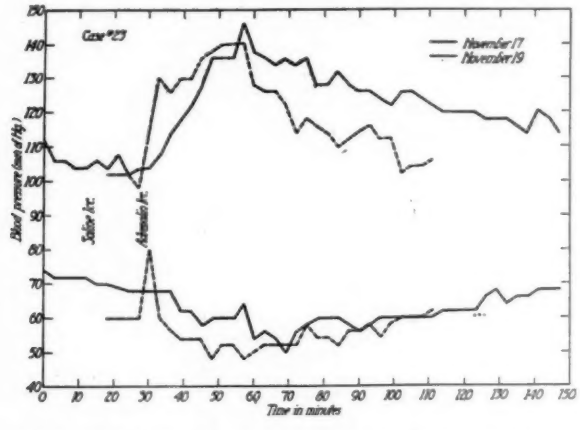


Fig. 1.—Showing the gradual increase and still more gradual decrease of systolic blood pressure after adrenalin in a normal person. On repeating the test, the pressure increased suddenly.

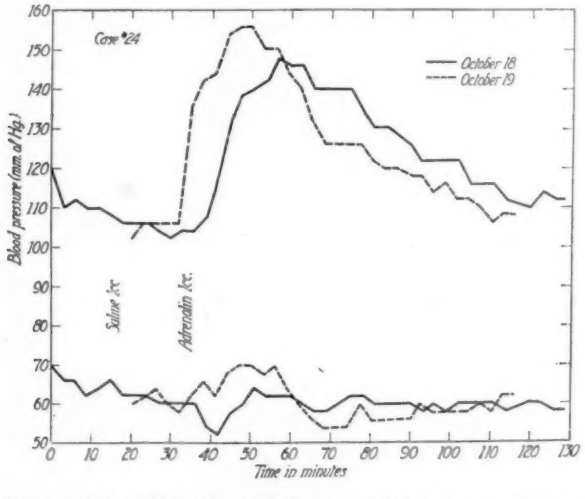


Fig. 2.—Showing a more sudden increase in a normal person. Also accentuation on repetition.

sibly it was due to fatigue of the mechanism which determined the response.

Although in the repeated tests the form of the diastolic blood pressure curve was fairly well retained, it might be modified by large or sudden increases of systolic pressures. Such systolic changes, how-

ever, did not necessarily affect the diastolic pressure. The increase in heart rate was not changed in the repeated tests.

B. *The Adrenalin Response in Pronounced Hypertension.*—Nine cases of this group showed a decrease of systolic blood pressure after adrenalin. This might or might not be preceded by a rise. On account of the spontaneous variations in the blood pressure of patients with hypertension it is not possible to describe any of these changes as adrenalin effects. Six cases showed a sharp systolic rise (Table III). In three of these six the increase was followed by a fall below the original level.

TABLE III

THE MAXIMAL INCREASES OF SYSTOLIC BLOOD PRESSURE (IN MM. HG AFTER A FIRST AND AFTER A REPEATED INJECTION OF 1 C.C. OF ADRENALIN INTO HYPERTENSIVE PATIENTS, AND THE TIME (IN MINUTES) CONSUMED OBTAINING THESE INCREASES*

| CASE NO. | FIRST INCR. | TEST TIME | REPEATED INCR. | TEST TIME | CASE NO. | FIRST INCR. | TEST TIME | REPEATED INCR. | TEST TIME |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 8 | 1 | 60 | 3 | 11 | 58 | 10 | 66 | 4 |
| 2 | 10 | 3 | 72 | 3 | 12 | 74 | 4 | 48 | 4 |
| 3 | 12 | 7 | 76 | 2½ | 13 | 100 | 3 | | |
| 4 | 20 | 13 | 94 | 4 | 14 | 88 | 3 | 64 | 2½ |
| 5 | 22 | 1 | 72 | 4½ | 15 | 30 | 3 | 42 | 4 |
| 6 | 6 | 7 | 44 | 3 | | | | | |
| 7 | 6 | 4 | 66 | 4 | | | | | |
| 8 | 16 | 2½ | 54 | 2½ | | | | | |
| 9 | 44 | 4 | 74 | 2 | | | | | |
| 10 | 18 | 4 | 66 | 2½ | | | | | |

*In the cases of the first column, the increase, which after a first injection is slight, is accentuated and the time is somewhat shortened after the repeated tests. In the second column the increase after the first injection is considerable. After the repeated injection it is not accentuated, but the time is somewhat shortened.

TABLE IV

MAXIMAL INCREASES OF SYSTOLIC BLOOD PRESSURE (MM. HG) AFTER A FIRST AND AFTER A REPEATED INJECTION OF 1 C.C. OF ADRENALIN INTO SIX CASES OF EARLY OR INTERMITTENT HYPERTENSION, AND THE TIME CONSUMED (IN MINUTES) TO OBTAIN THIS INCREASE

| CASE NO. | FIRST INCREASE | TEST TIME | REPEATED INCREASE | TEST TIME |
|---|---|---|---|---|
| 31 | 0 | 0 | 30 | 7 |
| 32 | 20 | 4 | 42 | 3 |
| 33 | 16 | 22 | 20 | 2 |
| 34 | 18 | 19 | 18 | 5 |
| 35 | 18 | 5 | 20 | 2½ |
| 36 | 20 | 19 | 36 | 2½ |

On fourteen patients with hypertension the tests were repeated at intervals varying from 12 hours to 30 days. In all of them the repeated test showed a sudden and intense increase of the systolic pressure. In the nine cases where the response to the first test had been indeterminate the contrast between the first and the repeated tests was most striking (Fig. 3). In one case the response to the first injection was so violent that the test was not repeated. In three cases

where the first reaction had been brisk, the response on repetition was greatly intensified (Fig. 4). In two cases the repeated response was slightly less but otherwise similar to the first one. When the test was repeated after 48 hours in case 14, the reaction was considerably diminished and case 6 failed to respond 24 hours after the first test. Both, however, gave an active response respectively 8 and 2 days after the first injection. The findings are summarized in Table IV and the protocol of a typical case is appended below.

A decrease of the diastolic pressure of from 8 to 34 mm. Hg occurred in 13 to 54 minutes. When the systolic pressure rose sharply the

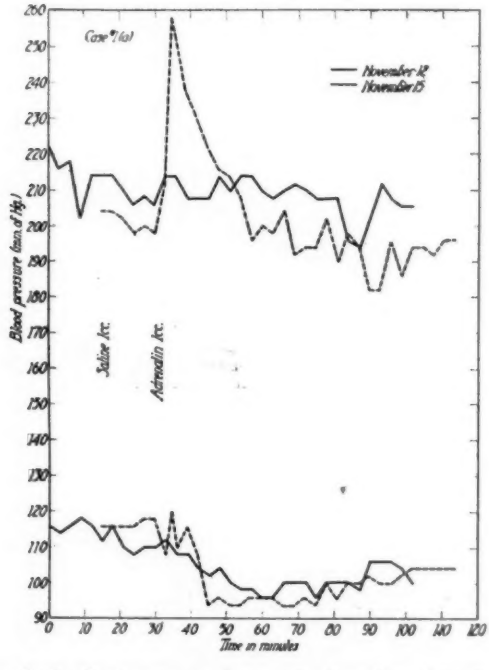


Fig. 3.—Showing lack of response to 1 c.c. of adrenalin when first administered to a hypertensive patient. On the repeated test three days later the injection was followed by an intense reaction with subsequent decrease to sub-initial level. Decrease of diastolic pressure.

diastolic fall was preceded by an increase corresponding to the systolic rise. The diastolic pressure changes were not as great as the systolic. The return to normal was so slow that in only two cases of the series did it occur during the period of observation. With repeated tests the diastolic response was but slightly modified except in the cases where the systolic pressure rose sharply. Then the diastolic, as in the first tests, showed a corresponding, moderate, transient increase. There was no evidence that the changes in the diastolic pressure are related in any way to those of the systolic pressure. Also in the repeated tests the diastolic pressure was slow in returning to normal. There was no

change in the diastolic reaction after repeated injections of adrenalin. The acceleration of the heart rate varied from case to case without relation to the changes in the blood pressure. When the tests were repeated no important change in response was observed, except during very severe systolic reactions. Then the pulse rate increased considerably for a few minutes. This was thought to be due to cardiac distress rather than to a direct adrenalin effect.

Thus the response in the patients with hypertension to first injections of adrenalin fell into two groups. In one no certain effect could be

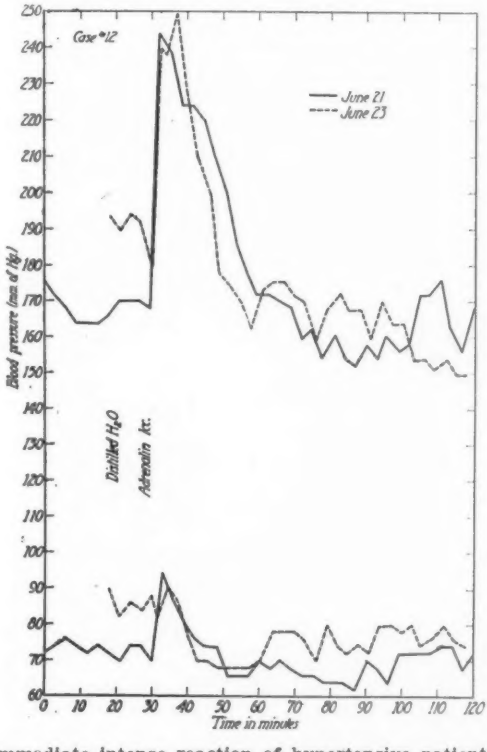


Fig. 4.—Showing immediate intense reaction of hypertensive patient to adrenalin. On repeating the test two days later, a similar response was obtained.

ascribed to adrenalin and in the other the response was intense. The reactions of the diastolic blood pressure and of the heart rate were marked by no division into groups.

The protocol of patient No. 2 is given in some detail as an example of the general reactions observed during the procedure.

### CASE REPORT

Mr. J. T., aged 47 years, was known to have had hypertension for one month. The hospital diagnosis was primary hypertension with some renal insufficiency. He was given adrenalin 1 c.c. (Fig. 3). This caused no definite change in his systolic blood pressure. Three days later the test was repeated. The systolic pressure now

rose 60 mm. Hg, in three minutes, and he felt very sick. He became pale and was very tremulous; for 20 minutes he had a severe headache. The elevated blood pressure immediately began to fall and in 20 minutes had reached the original level. Later it decreased an additional 20 mm. Also this time the diastolic pressure decreased, except for a slight increase while the systemic pressure was highest. As the systolic pressure decreased, the patient felt better, but all through the day he suffered from paroxysmal tremulousness. When the test was repeated the next day, a similar reaction followed.

Eighteen days after the initial injection no immediate systolic reaction took place; an increase of 30 mm. Hg half an hour later could not be considered an adrenalin effect as it fell within the spontaneous variations in hypertension. The following day there was no systolic change after adrenalin. The diastolic change was constant; a gradual decrease lasted through the period of observation.

C. *The Adrenalin Response in Cases of Early or Intermittent Hypertension.*—In the group designated by pronounced hypertension systolic pressures of 186 or over and diastolic pressures over 100 mm. Hg were

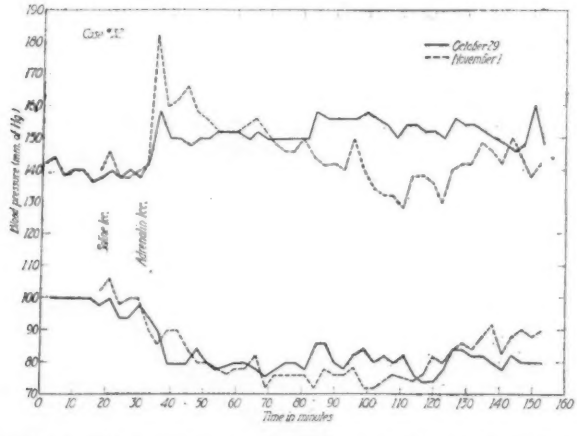


Fig. 5.—Showing slight response to adrenalin in a case of early hypertension. On repeating the test a sudden and intense response was obtained, though of smaller magnitude than in advanced hypertension.

found. The group designated by early or intermittent hypertension had diastolic pressures below 100, and highly variable systolic pressures, at times more than 150 and at others less than 130. The marked spontaneous variations of the systolic pressures frequently obscured the results of the injections. The injection of adrenalin was always followed by an increase in systolic pressure, but this exceeded 20 mm. in one instance only. Although in three cases the pressure subsequently sank below the initial level, this decrease was within the normal limits of spontaneous variations. The increase in pressure was much less than was usual in normal persons. When the tests were repeated 2 to 4 days later this group showed a marked change in response, which was now sharp and immediate although less than in advanced hypertension. (Fig. 5, Table IV.) The diastolic pressure changes in the individuals with hypertension differed from those in normal persons mainly in

that they returned more slowly to normal. In this respect the cases of intermittent hypertension distributed themselves evenly; three did and three did not present normal diastolic pressures at the end of the test.

## DISCUSSION

A. *The Normal Variation in Adrenalin Response.*—Our results, which show that the systolic blood pressure increased from 15 to 38 mm. after the subcutaneous injection of adrenalin, agree well with those of Bauer,[4] Brems,[16] and others. I have found in the literature of well documented researches no investigation on the constancy of the test when repeated in the same person. Almost everyone who injected adrenalin repeatedly

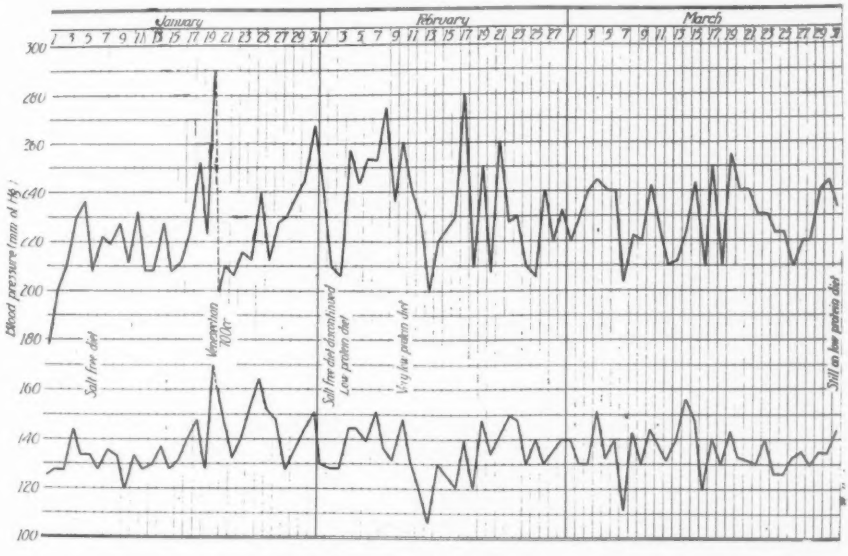


Fig. 6.—Showing diurnal variations of blood pressure in a case of severe hypertension of ten years' standing. The systolic pressure shows much greater variations than does the diastolic.

introduced some factor between the two injections and ascribed any change to this factor. Brems[17] worked with calcium and the adrenalin test; Billigheimer[18] with protein diet; Mahler[19] with glycosides; Peabody[7] with infections.

I had observed the decrease of the diastolic pressure on patients before I learned of it from the literature. Independently Dr. Ulrich suggested that this effect was due to a peripheral vasodilatation. Later we found that Bauer,[4] Hotz,[20] Brems[17] and others had observed a lowered diastolic pressure and had already suggested a similar interpretation.

The normal response to adrenalin is characterized by a more or less rapid, but rarely sudden, increase of systolic blood pressure, followed by a somewhat slower return to normal level, and by a decrease in

diastolic pressure which usually returns to normal well before ninety minutes. When the test is repeated the increase in blood pressure is more sudden and intense, but the general configuration of the blood pressure curve is not affected.

B. *The Response of the Hypertensive Patient to Adrenalin.*—It is now well known that even in advanced hypertension the blood pressure may vary considerably. Figure 6 illustrates the daily variations of blood pressure in a patient who had had hypertension for ten years.

It seemed worth while to make a mathematical observation to ascertain whether this difference in variability of blood pressure between normal persons and hypertensive patients was mathematically a true difference or whether it was only apparent. This was done under the direction of Dr. Scammon in the Department of Anatomy.

For this purpose 36 blood-pressure readings were obtained from two patients with hypertension and two controls (Table V). The readings were taken about 12 at a session, at two-minute intervals, the various series being taken on different days, but under identical conditions so as to include both the minute-to-minute and day-to-day variations.

The average of the readings was calculated for each person as well as the probable error of the average, and the standard deviation was then calculated in the usual manner and its probable error determined.

Each control was now compared with the two persons with hypertension and the difference between the standard deviations was calculated as was also the probable error of this difference.

The standard deviation is an expression of the variability of the blood pressure, and in order to show a real difference, the difference between the standard deviations

$$\frac{S\ D_h - S\ D_n}{\text{Error } (S\ D_h - S\ D_n)} = \text{should be above three,}$$

where $S\ D_h$ = standard deviation of the pressure in hypertension, and $S\ D_n$ = standard deviation of the normal pressure. It will be seen from Table V that in all four cases this ratio exceeded three; the variability of blood pressure in patients with hypertension mathematically exceeded that of the controls. This tendency to spontaneous changes and the excessive reactions to stimuli had to be taken into consideration when evaluating the response to adrenalin. It is not surprising, therefore, that the patient with hypertension reacted with excursions of his blood pressure far in excess of those seen in normal persons, in some cases only after a preliminary administration of the drug. This might be followed by an abrupt fall to a sub-initial level.

With a few exceptions the curves obtained from patients with hypertension were easily distinguished from the normal curves. One patient with hypertension (No. 3) had after the first injection a slowly but definitely increasing blood pressure, while in one of the normal in-

TABLE V

SHOWING A TRUE MATHEMATICAL DIFFERENCE BETWEEN THE VARIABILITY OF SYSTOLIC BLOOD PRESSURE IN NORMAL AND HYPERTENSIVE PERSONS*

| NAMES | NORMAL | | HYPERTENSIVE | | DIFFERENCE BETWEEN STANDARD DEVIATIONS | PROBABLE ERROR OF DIFFERENCE BETWEEN ST. DEV. | RATIO OF DIFFERENCE AND OF PROBABLE ERROR OF DIFFERENCE BETWEEN ST. DEV. |
|---|---|---|---|---|---|---|---|
| | AVERAGE AND PROBABLE ERROR OF AVERAGE | STANDARD DEVIATION AND PROBABLE ERROR OF ST. DEV. | AVERAGE AND PROBABLE ERROR OF AVERAGE | STANDARD DEVIATION AND PROBABLE ERROR OF ST. DEV. | | | |
| Normal A—Hypertension X | 114.9 ± 1.29 | 3.40 ± 0.27 | 167.5 ± 1.88 | 13.60 ± 1.07 | 10.20 | 1.10 | 9.28 |
| Normal A—Hypertension Y | 114.9 ± 1.29 | 3.40 ± 0.27 | 193.1 ± 2.16 | 7.61 ± 0.60 | 4.21 | 0.66 | 6.38 |
| Normal B—Hypertension X | 109.3 ± 1.22 | 4.27 ± 0.34 | 167.5 ± 1.88 | 13.60 ± 1.07 | 9.33 | 1.12 | 8.33 |
| Normal B—Hypertension Y | 109.3 ± 1.22 | 4.27 ± 0.34 | 193.1 ± 2.16 | 7.61 ± 0.60 | 3.34 | 0.69 | 4.84 |

*All figures on the basis of 36 readings.

dividuals (No. 28) the wave rose to a high maximum within a few minutes of the injection of adrenalin. During the repeated tests several of the normal controls gave an intense response. But in these cases the subsequent decrease was slower than in hypertension and the blood pressure did not reach the sub-initial levels seen in the patients with hypertension. While no single feature of the reaction was of absolute value in determining the difference between the normal response and that in hypertension, the reaction in the two groups was on the whole strikingly different.

In the cases of hypertension the response of the diastolic pressure was not grossly different from that of normal individuals. Generally, however, there was a greater lag in its return to the initial level.

A striking feature in the analysis of the tests on patients with hypertension was the division into two groups: in one (which we shall call Group A) the response of the systolic blood pressure was insignificant and formed a marked contrast to the intense response obtained when the test was repeated about forty-eight hours later. In the other group (which is designated as group B) the response was marked both to the first and to subsequent injections. There were no clinical features by which the two groups could be distinguished from one another. It was particularly noted that the response was not determined by the amount of kidney damage.

In analyzing the material the groups were easily separated, though some of the patients who gave an insignificant response did show a small sudden rise of blood pressure immediately after the injection. The possibility that this was spontaneous or due to psychic causes could not be excluded.

In early or intermittent hypertension the conditions were intermediary between the two previous groups. The response to a first injection was approximately as in the persons with hypertension of group A, and less than in the normal person. On repetition the response was markedly accentuated but less than in the patients with hypertension of Group A. In the repeated tests the average increase of blood pressure after adrenalin was 83 per cent over the increase after the first injection; in marked hypertension of Group A it was increased 412 per cent, and in normal persons it was 21 per cent.

The maximum reading was reached sooner in advanced than in early hypertension and sooner in early hypertension than in normal persons. After the repeated injection the maximum reading was reached as soon in early hypertension as in advanced hypertension.

Also the variations in blood pressure after the first and the repeated tests were analyzed for the purpose of determining to what extent the change in response was mathematically true. For this purpose the average blood pressure was computed from about thirty readings after the giving of adrenalin and the probable error thereof was determined.

The standard deviation from this average, that is, the variability of the pressure after adrenalin, was calculated with its probable error. This was done both in the first and the repeated tests, and the two standard deviations were compared. If the standard deviations (that is, variability of blood pressure, in this case increase of blood pressure) should be significantly greater in the repeated than in the first test, the difference between the standard deviation of the first and the repeated tests should exceed three times the probable error of this difference.

This difference was significant in the cases of hypertension of Group A where there was a marked contrast between the first and repeated tests and in one case of intermittent hypertension, but not in the controls nor in the persons with hypertension of Group B who reacted well to the first injection; nor in the most cases of early or intermittent hypertension.

*The Mechanism of the Adrenalin Response in Hypertension.*—In the discussion by other authors of the adrenalin reaction in hypertension various interpretations were given of the results obtained. Investigating these results two questions presented themselves: Is the reaction, as obtained in hypertension, specific for that condition; and is there in hypertension any one demonstrable factor upon which the reaction depends?

I believe that the response characteristic of hypertension is the sudden intense increase of systolic blood pressure, and that this response is in some hypertensive individuals obscured by the lack of reaction to the first injection. This will be discussed below. I found it also in some normal persons, though the excursions were not quite of the magnitude observed in individuals with hypertension. Goetsch[5] and others obtained a similar response in hyperthyroidism. This I could confirm. Peabody[7] found it in certain cases of functional cardiovascular disease. This sudden intense response is by some considered characteristic of sympathicotonia, and without accepting or denying that doctrine one must admit that the response in hypertension may also be found in conditions other than hypertension.

The factors upon which the sudden increase in blood pressure depends in patients with hypertension have been considered. The reaction is not dependent upon the height of the blood pressure at the time of the test or on the general level of blood pressure of any individual.

Patients suffering from hypertension with equally high blood pressures, either did not respond or showed an intense increase of pressure to the first injection of adrenalin. The intense reaction might be absent when the blood pressure was elevated, but might occur in persons suffering from hypertension with pressures at many varying levels and might be found in patients with hyperthyroidism where the systolic pressure was normal. The response was intense not only as regards the

increase of pressure but also as to the suddenness with which this pressure was obtained.

One patient (No. 16) reacted to adrenalin like a case of hypertension, and the first injection was followed by no certain blood pressure changes. At the subsequent test an intense rise occurred. He had much clinical evidence of hypertension and a blood pressure which varied considerably from time to time and from beat to beat, but the systolic variations were between 108 and 135.

The response does not depend upon demonstrable cardiac or renal factors. It was found both with and without cardiac enlargement. Two cases of early nephritis reacted like normal persons. A case of advanced nephritis with a very high blood pressure gave a response as intense as any other hypertensive patient. Kylin[21] has stated that the blood calcium influences the blood pressure and the adrenalin reaction. In one patient where the parathyroid glands had been accidentally removed, and where the blood calcium could be regulated at will, I had an opportunity of examining the blood calcium both in relation to the height of the blood pressure and the adrenalin reaction. The three factors were not related. The adrenalin test was originally introduced as a diagnostic test for sympathicotonia and it might be asked if the intense reaction obtained in hypertension indicates that state. Adrenalin affects a number of functions, ordinarily under the control of the sympathetic nervous system: for instance, in the cardiovascular system, the blood pressure, the pulse rate, the conduction of impulses in the heart and the irritability of the cardiac muscle; but only the blood pressure response is increased in hypertension. If by sympathicotonia we are to understand the single manifestation of increase in blood pressure, then the response in hypertension could be considered sympathicotonic, but if sympathicotonia embodies a general hypersensitiveness to agents affecting the sympathetic nervous system, then this isolated sensitiveness of the systolic blood pressure cannot be so considered.

The view is prevalent in the literature that adrenalin given subcutaneously causes a peripheral vasoconstriction. I was unable to correlate this opinion with the findings of a decrease in diastolic pressure and on Dr. Ulrich's suggestion I was led to assume a peripheral vasodilatation. In a later study of the literature it was found that many authors have confirmed this view.

Kahn[22] noticed that in pulse tracings after adrenalin the pulse curve dropped more quickly than in controls, showing that the artery emptied faster. Bayliss[23] showed that when the intra-aortic pressure increased a generalized vasodilatation occurred. This reflex took place through increased aortic pressure and not through increased intracranial pressure.

Von Anrep[24] found by plethysmographic observations that the limb volume passively followed the pressure in the brachial artery, and Rosenow[25] believed the dilatation was a simple passive process caused by an increased load of blood thrown into the limb circulation, but Bayliss'[23] observation, that he obtained vasodilatation in the head and neck of a dog which was supplied from another heart-lung preparation, has shown that the vasodilatation was a reflex, and von Anrep[26] was unable to obtain any direct local reaction to changes of blood pressure by changing the pressure in a closed carotid artery.

Bauer in 1912[4] demonstrated that the low diastolic pressure meant peripheral vasodilatation, but his finding was frequently overlooked. Some authors when acquainted with Bauer's argument maintained their belief in vasoconstriction but transferred the site to the splanchnic area (Bauer,[4] Rosenow,[25] Pophal,[27] Hotz,[20] Horning,[28] Lyon,[29] Brems,[17] and others). This view was introduced into the German literature by Biedl[30] who in his *Innere Sekretion,* quoted from Oliver and Schäfer.[31] These authors had stated: "It may fairly be assumed that although we are unable to record any plethysmographic observations on the intestine, the great rise of blood pressure which invariably follows the injection of the extract is in all cases due very largely to the contraction of the arterioles of the splanchnic area." The experimental data underlying this assumption were not conclusive, and confirmatory evidence has not been observed in the later literature.

The systolic blood pressure is the outcome of two main factors: the velocity given to the blood stream by the contraction of the heart muscle and the resistance of the peripheral vascular system. The former acts during systole only, the latter during both systole and diastole. In the adrenalin test there is an increase of the pressure during systole only while there is no increase during diastole. Therefore, the increase of blood pressure must be due to the factor which acts during systole, the cardiac contraction. Dr. Ulrich originally suggested this mechanism and in a later study of the literature many authors were found to confirm this view. When auscultating the aortic area after giving adrenalin, the first sound was greatly accentuated but not the second, as would have been expected if the heart were working against increased peripheral resistance. I interpreted this increase of the first aortic sound as being due to augmented muscular vigor. Gottlieb[32] on the basis of adrenalin effect on the chloralized heart called attention to the importance of the cardiac factor in the reaction and in 1900 showed a tremendous augmentor effect of adrenalin on the isolated heart lung preparation.[33] Clough[9] also expressed the opinion that we are dealing primarily with a cardiac reaction rather than a peripheral one.

Lee Gunning[34] observed that in a dog, where the blood pressure varied in the different arteries, adrenalin produced the same absolute increase in all arteries irrespective of the initial pressure. A peripheral mechan-

ism might have been expected to produce a less regular response. Pilcher[35] caused a rise in the diastolic pressure by producing vasoconstriction of the peripheral circulation. Von Anrep[36] found that the secondary rise of blood pressure after splanchnic stimulation, which he attributed to liberation of adrenalin from the adrenals, bore a distinct relation to the tone of the heart. He also showed the heart's action to be the cause and not the result of the blood-pressure change; especially as hearts which worked against a peripheral resistance were not stimulated to greater efforts as were adrenalized hearts.

Thus confirmatory evidence is not lacking that in the clinical adrenalin response we are dealing essentially with a cardiac functional test.

All these patients with hypertension had blood pressures which were subject to great variations and I finally concluded that adrenalin response in hypertension is a manifestation of the general instability of the pressure in hypertensive individuals. This agrees with the finding that persons who had no hypertension, but who had given this kind of response, also had unstable vasomotor systems.

*The Lack of Response to the First Injection in Some Hypertensives.*—It is difficult to explain why an indeterminate response was obtained in some patients with hypertension when adrenalin was administered the first time. Clinically these cases differed in no way from those of the other group.

Some physiological experiments seem to resemble this reaction of hypertension. Sawitsch and Speranskaja-Stepanowa[37] found that cats with experimentally elevated pressures responded to adrenalin with irregular increases or even decreases of blood pressure. Gottlieb[33] investigated the cardiac reaction to adrenalin while the heart of the heart-lung preparation was working first against increased and thereafter against normal resistance. The reaction was much smaller when the resistance was higher. Cannon and Lyman[38] found that the initial peripheral tension determined the blood-pressure excursion after adrenalin; as the pressure increased, the excursion decreased and might even become negative. These findings were confirmed by Hartman.[39] Lyon[40] stated that "when the resting levels differ, the blood-pressure response to uniform doses of adrenalin varies, the magnitude of the disturbance diminishing as the resting level rises." In all these experiments the reaction to adrenalin was diminished when the heart worked against increased pressure, but clinically the same type of reaction was seen in case No. 16 where the blood pressure was within normal limits.

## SUMMARY

1. It appears from the literature that the response to adrenalin in the patient with hypertension differs from that of the normal person, but the evidence as to the variations in response is contradictory.

2. Under approximately standard conditions series of subcutaneous injections of 1 c.c. of adrenalin were given to a number of normal persons, patients with hypertension, and others in whom the reaction was thought to throw light on the phenomena observed in hypertension.

3. Persons with normal cardiovascular systems responded with a slow rise and a subsequent slower decrease of pressure. While the height of the excursion was but slightly accentuated after subsequent injections, the time consumed in reaching the maximum height of the pressure was markedly shortened.

4. The cases of hypertension fell into two groups which were clinically indistinguishable. In the first group no definite change could be ascribed to the first injection of adrenalin, while the other cases of marked hypertension responded with a brisk and intense increase of systolic blood pressure. When the test was repeated all the patients with hypertension responded with intense rises of pressure. In cases of early or intermittent hypertension the findings were like those of the former group of advanced hypertension, but less pronounced.

5. Statistically it was found that the ratio of the difference and of the probable error of difference between the standard deviations from the average readings following the first and the repeated injections of adrenalin was significant in the first group, in those hypertensive patients in whom the response was absent on the first injection.

6. The diastolic pressure decreased after all the injections but the time required to return to normal was longer in the patient with hypertension than in the normal person. It was not influenced by repetition of the test.

The increase in heart rate and the occurrence of cardiac irregularities were not influenced by the state of hypertension or by repetition of the test.

7. The blood pressure reaction of adrenalin in hypertension did not depend on the level of the blood pressure, the size of the heart, presence or absence of kidney disease, or the level of the blood calcium. No satisfactory explanation could be offered for the absence of response in some individuals with hypertension or for the change in response between first and subsequent tests.

8. The clinical adrenalin reaction is not due to peripheral vasoconstriction. In fact a vasodilatation is present which indicates that the systolic rise is of cardiac origin. The intense increase in the patient with hypertension is thought to be related to the general instability of the hypertensive blood pressure. This instability is briefly discussed and considered mathematically.

This work was done under the direction of Dr. Henry Ulrich to whom I am gratefully indebted for many practical suggestions.

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# ELASTICITY (EXTENSIBILITY) OF THE AORTA OF HUMAN BEINGS*

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A FAIR number of investigations have been made on the physical properties of the aorta of human beings. Most of these studies have been concerned with the elasticity of strips of the aorta, whereas some were directed toward the properties of internal pressure. By elasticity of vascular tissue is meant its power of yielding to a force and of resuming the original form when that force is removed. Herringham and Wills[1] determined that practically all aortas, when placed in physiological saline solution for five minutes, after they had been stretched with weights up to 200 gm., returned to their original form, and, therefore, that aortas are almost perfectly elastic. They also showed that the elasticity of the aorta depends chiefly on the amount of elastic and of connective tissue in the media and their reciprocal relations.

The following data of previous investigators have been accepted by us as being established: Post-mortem rigidity of the muscular media is negligible in the aorta of human beings.[3] Until putrefaction is far advanced the curve of elasticity of any aorta remains the same.[5] Only a very small amount of elasticity is lost over a long period of time (months) when the strip of aorta is kept constantly in physiologic saline solution, when the stretching is performed in that solution. The imperfection of elastic resiliency and the increase in extension are both dependent on the amount and the duration of the stretch.[7] Curves taken slowly (a half hour) are of the same form as those taken rapidly (two to three minutes[5]). Longitudinal strips taken from different sections of the aorta give the same curves and one strip is honestly representative.[2] The elasticity of longitudinal strips is less marked and less important than that of transverse strips.[2, 5]

That elasticity is dependent on age has been definitely determined, and it has been stated that elasticity (extensibility) increases from birth to the age of twenty years, after which there is a decline toward zero in senescence. Parallelism has not been established between the condition of the heart, general nutrition of the body or existing diseases and the elasticity of the aorta. Most authors agree that parallelism between loss of elasticity and degree of arteriosclerosis does not exist.

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## OBJECT AND METHOD OF STUDY

We have devised a simple apparatus for measuring the extensibility of approximately identical, transverse strips of the aorta, and with it have determined this property as exemplified in 100 aortas of human beings. The object in view has been to correlate this property with age, sex, blood pressure, degree of visible arteriosclerosis, thickness of the wall of the vessel, and cause of death. The first portion of the opened aorta was removed from the unembalmed body and was placed in physiological saline solution, in which it remained for a variable length of time, usually a few hours. The piece of aorta was then placed, endocardium downward, on a flat board and the loose fascia adjacent to the adventitia was stripped off. A brass plate, 6 cm. long and 1 cm. wide, held with a handle, was placed on the vessel transversely, just above the attachment of the aortic valve, and pressure was applied evenly while with a sharp razor blade the section thus fixed by the plate

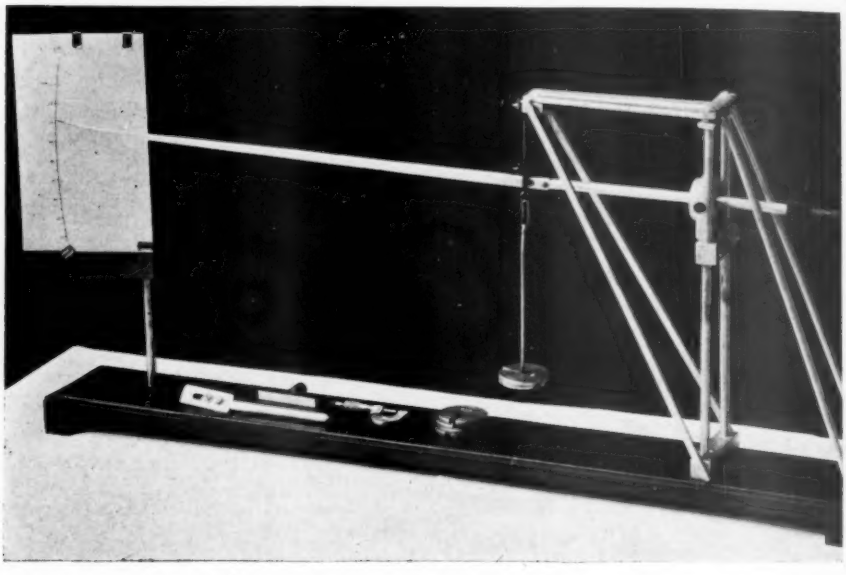

Fig. 1.—Apparatus for determining elasticity of tissue.

was cut out. An effort was made to avoid inclusion of calcified regions if such were present. The thickness of the strip obtained was measured in the middle and toward each end with a caliper micrometer; care was taken to close the calipers with uniform snugness, and each measurement was taken three times. The average of these three readings was taken as the thickness of the portion calibrated, and the average of the thicknesses of the three portions measured was taken as the thickness of the strip for purposes of comparison. The strip was then placed in the clamps of our apparatus, so that without weight applied the section of the strip between the clamps measured accurately 4 cm. Weights of 50 gm. each were then hung successively on the lower clamp. With the first weight and with each additional weight the strip was allowed to stretch for half a minute before a reading was made on a magnified scale. Six weights were used with each test, resulting in six readings for each strip. In making the tests we endeavored to minimize errors of personal equation by using exactly the same technic with all strips.

Fig. 1 is a photograph of the apparatus used, a brief description of which follows: On a rectangular wooden base board is mounted at one end a rigid aluminium

gallow and at the opposite end a vertical reading scale. At a properly selected point on the vertical portion of the gallow is constructed a fulcrum for an aluminium balancing bar with as little friction as is practicably possible. One arm of the bar extends in the form of a pointer toward the reading scale. Integral with this arm is a fastening clamp situated directly under a similar fastening clamp at the distal end of the horizontal portion of the gallow. On the arm, immediately beneath the clamp, is attached a ring to which the loads can be applied. Proper initial balance of the bar is secured by an adjustable counterweight on the opposite arm. The reading scale is adjusted in such a position that when the pointer is directed to the zero mark, at the upper end of the scale, the length of the strip of aorta between the two fastening clamps is exactly 4 cm. Direct determination of increasing distances between the clamps results in magnification of the scale, rendering the readings accurate to one-tenth of a millimeter.

The data concerning age, sex, average blood pressure, clinical history, cause of death and degree of visible arteriosclerosis of the aorta were recorded in each case. Arteriosclerosis was graded grossly by inspection of the entire aorta and the degree of sclerosis and the extent of the distribution were graded separately and then combined. This grading is naturally variable, depending on the discretion of the grader, but as far as possible it was done by the same person.

By plotting the results of the stretching on graph paper, using for abscissas the successive changes in weight, and for ordinates the corresponding increments of length, it was seen that the resulting line drawn formed a curve approaching the hyperbola without having the mathematic function of this figure. This result corroborated the work of previous investigators.[1, 4, 5, 8]

## OBSERVATIONS

*Relation of Elasticity to Age.*—The results were plotted on graph paper for each weight used (50, 100, 150, 200, 250 and 300 gm.), the ages in years of the subjects being used as ordinates and the increments of length of the strips as abscissas. From the age of seven years to that of twenty-seven years there was an increase in extensibility, and after the age of twenty-seven years there was a steady decrease. There were, however, only seven instances in which the subjects were aged from seven to twenty-seven years inclusive. The results with strips from subjects aged more than twenty-seven years grouped themselves fairly closely about a straight line. The greatest spread occurred with the smallest weight applied, 50 gm. The increase in extensibility before the age of twenty-seven years was more rapid than the decrease after that age. Figure 2 is a graph of the result obtained when the figures recorded with the 100-gram weight were plotted.

*Relation of Elasticity to Sex.*—The results were next plotted on graph paper for each weight used in the same manner as in the preceding graphs, red dots representing females and black dots representing males. The red and black dots were so distributed that there appeared to be no difference in degree of extensibility with sex. This is opposed to the results of Herringham and Wills, who stated that at every age aortas of females are less elastic than those of males.

*Relation of Elasticity to Blood Pressure.*—For comparison the average of the diastolic blood pressures obtained while the subjects were in

hospital were used. The subjects were divided into age groups for the study of this feature as follows: ages seven to twenty-nine years inclusive, nine subjects; ages thirty to thirty-nine years inclusive, twelve subjects; ages forty to forty-nine years inclusive, thirteen subjects; ages fifty to fifty-nine years inclusive, twenty-two subjects; ages sixty to sixty-nine years inclusive, twenty-six subjects, and ages seventy years or more, eighteen subjects. This grouping was made in order to minimize the influence of age in this consideration. Within each of the age groups the subjects were arranged serially according to the height

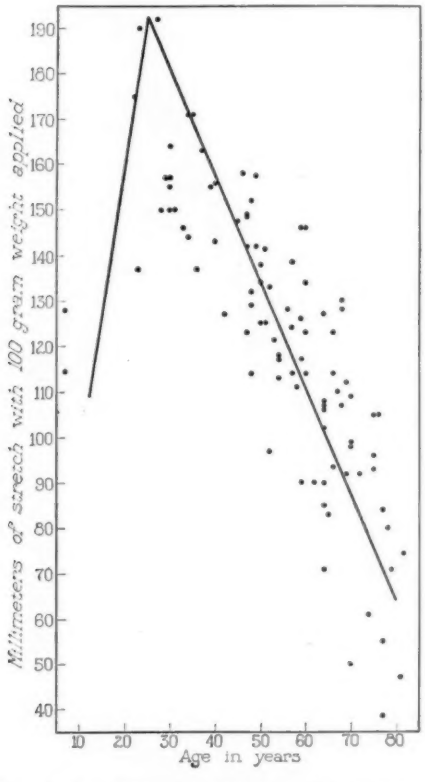


**Fig. 2.—Relation of elasticity of strips of aorta to ages of subjects.**

of the diastolic blood pressure. A study of this compilation did not reveal any relation between extensibility and diastolic blood pressure.

*Relation of Elasticity to Degree and Extent of Arteriosclerosis of the Aorta.*—In this study the subjects were arranged within each age group according to the classification of arteriosclerosis adopted, and the stretch of the strips with each weight was set down. In the age group thirty to thirty-nine years inclusive (twelve subjects) there was increased extensibility with increased amount of sclerosis, but in the other groups there was no apparent relation between extensibility and sclerosis. It

seems fair to conclude, therefore, that the elasticity of the aorta is not influenced parametrically by the sclerotic changes present, when the extensibility is determined of a strip of the aorta which is not involved in calcification. Calcification obviously would completely abolish elasticity.

*Relation of Elasticity to Thickness of Wall of Aorta.*—The results were plotted on graph paper for each weight applied, the abscissas used being the figures expressing the thickness of the strips as determined in the way already mentioned, and the ordinates used being the increments of stretch. The dots showed such a spread as to make it apparent that thickness does not play a part in the extensibility of the strip.

*Relation of Elasticity to Clinical History and Cause of Death.*—A relation was not apparent between extensibility and the nature of disease or diseases causing death.

## SUMMARY AND CONCLUSIONS

An apparatus has been devised for measuring the extensibility of linear strips of the unembalmed aorta.

The extensibility of linear strips of 100 aortas of human beings was measured.

The curve drawn on graph paper, on which the results of these measurements were plotted, resembles a hyperbola without having the mathematical function of this figure.

The extensibility of linear strips of the aorta increases from childhood to the age of twenty-seven years. After the age of twenty-seven years it steadily decreases, irrespective of sex, diastolic blood pressure, degree and extent of grossly estimated arteriosclerosis (calcified areas being excluded), thickness of the wall of the aorta and cause or causes of death.

These facts do not necessarily mean that the elasticity of the aorta as a whole is greater in young adulthood than in childhood, because the linear strips used were all of the same size, and we did not consider the ratio of the size of the strip either to the circumference of the aorta or to its total area. The best way to determine the elasticity of the aorta as a functioning structure would be by studying the properties of internal pressure. Such an investigation would involve the variables of blood pressure, volume output of the heart per beat and total volume of blood at various ages; this would be extremely difficult and complicated. However, after physical maturity has been reached, these variables as well as the change in the size of the aorta, are not so pronounced from young adulthood to old age. Therefore the results obtained in this investigation might be applied to the elasticity of the aorta as a whole after maturity, if it were not for the fact that areas of calcification have been eliminated in the strips used; these would

necessarily affect the elasticity of the aorta as a whole. The conclusions reached from this study apply only to linear strips of standard size which do not contain regions of calcification.

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# POLYPOID FIBROMA OF THE LEFT AURICLE (SO-CALLED CARDIAC MYXOMA) CAUSING A BALL-VALVE ACTION

## WITH REPORT OF A CASE*

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MEDICAL literature contains a fair number of case reports of primary cardiac tumors designated as myxomas. The large majority of these rare tumors have been located in the auricles, the left auricle having been a far more frequent site than the right auricle. Of all the primary cardiac tumors, myxomas (so-called) are the most common. The literature, as reviewed by Karrenstein,[1] Nowicki,[2] Perlstein,[3] Beck and Thatcher,[4] Goldstein,[5] and more recently by Bradley and Maxwell,[6] contains less than seventy-five reports of tumors of this type. The following case is reported in the hope that the clinical observations and pathologic findings, when added to the previous contributions may be of value in working out some means of ante-mortem diagnosis.

### CASE REPORT

The patient (Med. No. 33379) a white, Canadian-born housewife of forty-four years, entered the Medical Service of the Peter Bent Brigham Hospital as an ambulance case. Her chief complaint was of fainting attacks. The family history was not remarkable and gave no evidence of cardiac or of neoplastic disease. Her habits were of interest in that she was quite active for a woman of her age and swam a great deal. There had been several attacks of tonsillitis during the third decade. There was no history of previous circulatory symptoms, heart disease or of rheumatic fever. In the six weeks preceding entry there had been a loss of weight amounting to thirteen pounds.

The patient was quite definite in stating that she felt well and strong until six weeks before entry. At this time she experienced a moderately severe upper respiratory infection which, however, did not cause her to go to bed. In addition to a cough and yellowish sputum she noted rather marked substernal pain associated with her respiratory movements. Following recovery and during the fifth week before admission she resumed her swimming, and fainted for the first time upon coming out of the water. Somewhat alarmed, she stopped her housework and rested at home, but felt no need of going to bed. During the next four weeks she fainted four times and it was noted that each attack occurred while she was standing. It was known that her teeth needed attention, and three were extracted at home. Fainting did not occur again.

One week before admission moderate dyspnea developed and edema of the ankles was noted. The appetite, previously excellent, became poor; there were frequent dull frontal headaches and there was a marked increase in the urinary output. The patient had been in bed for four days when first seen; during this period the dyspnea and edema had increased, and cyanosis of the lips and finger nails appeared.

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She became definitely orthopneic and complained of her extremities feeling cold. Treatment during this last week had consisted of bromides and of an unknown quantity of digitalis given by a local physician.

Physical examination shortly after entry revealed a well-developed and well-nourished woman of middle age with only moderate dyspnea, orthopnea and cyanosis. She complained of persistent nausea and vomited twice during the examination. The rectal temperature was 101° F., pulse 110, respirations 30 per minute. The skin was warm, moist and clear. The eyes were quite normal. Ophthalmoscopic examination revealed no changes in the retinal arteries. The radial pulses were equal, synchronous, weak, and of normal rhythm. The vessel walls were elastic. The blood pressure, in the sitting position, was 65 mm. systolic, 57 mm. diastolic.

The apex impulse of the heart was felt, but not seen, 9.5 cm. to the left of the midsternal line in the fifth interspace and was forceful and sharply localized. Over this area there was a definite systolic thrill, remarkable in that it was only palpable over an area approximately 3.5 cm. in diameter. The heart was but slightly e..

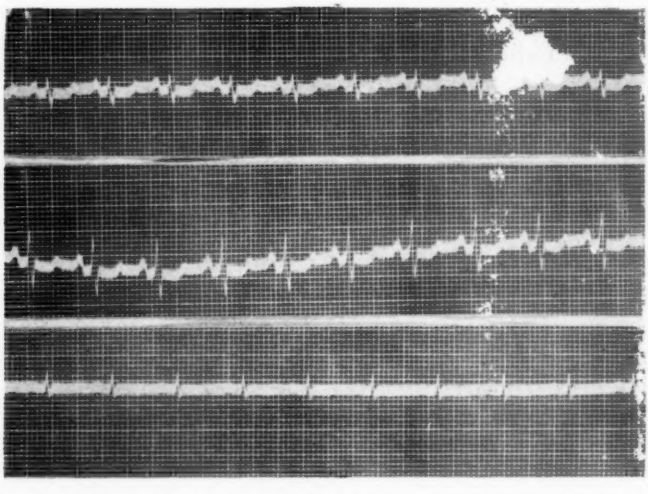


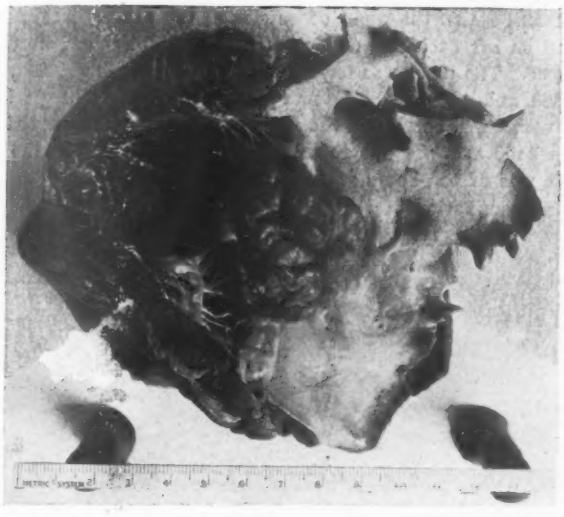
Fig. 1.—Electrocardiographic tracing from the three customary leads taken Sept. 27, 1928. Rate 120. The electromotive force is somewhat low.

larged, the left border of dulness being 10.5 cm. to the left of the midsternal line in the fifth interspace, and the right border of dulness 2.5 cm. to the right. A soft systolic murmur was heard at the apex, together with a short presystolic rumble which did not obscure the first sound. There was no suggestion of gallop rhythm.

The lungs were resonant, except at the posterior bases where there was slight dulness, this being more marked on the left. The breath sounds were vesicular throughout, but were noted to be somewhat distant over the left base. The fremitus was slightly diminished over the same area. There was no alteration in transmission of the spoken and whispered voice sounds. A few fine crackling rales were heard over both lung bases. The liver was palpable 3 cm. below the right costal margin and was rounded, smooth and quite tender, but did not pulsate. The hands and fingers were cyanotic and cold. The legs showed marked pitting edema extending up to the knees. Moderate sacral edema was also present.

Only one specimen of urine was examined, this being light straw in color, alkaline, and containing no albumin or sugar. Only a few leucocytes were seen in the sediment. Examination of the blood showed a hemoglobin value of 80 per cent (Tallqvist); red cells 5,510,000 and white cells 21,400 per c.mm. The stained smear

gave the appearance of very slight central achromia and of a normal number of platelets. Polymorphonuclears 74 per cent, lymphocytes 20 per cent, large mononuclears 4 per cent, undetermined 2 per cent. An electrocardiogram taken three hours after entry showed a sinus tachycardia, rate 120. (See Fig. 1.) There was a somewhat abnormal form of ventricular complex and the appearance of moderately



—A photograph of the opened heart fixed in Kaiserling's solution, showing the position of the tumor mass.

Fig. 3.—A photograph of the fixed specimen with tumor lifted above the mitral valve, showing the pedicle attachment.

low electromotive force. There was no evidence of digitalis intoxication. The blood Wassermann was weakly positive. The Hinton precipitin test for syphilis performed upon the same serum was negative.

On the basis of the above findings, the diagnosis of mitral stenosis and congestive heart failure was made, and the patient was placed upon the Karrell diet and given

morphine. In view of the vomiting and of the history of digitalis having been taken just before entry, a total of only 0.3 grams of digitalis leaf was given during the afternoon. Under the rest and morphine her temperature, pulse and respirations all became lower and her condition seemed greatly improved. There was some vomiting about 6:00 P.M. Within eight hours after admission the temperature had fallen to normal, the pulse from 110 to 95, and respirations to 20.

When seen at 12:30 A.M. the night of admission the patient was sleeping quietly, being propped up on her back rest and pillows. The respirations were slow, regular and normal in type. The pulse was improved in volume, quite regular, rate 90. She was not awakened and the blood pressure was not taken. The patient continued to sleep for the next three hours and the night nurse found her condition unchanged at 3:20 A.M. At 3:30 A.M. she was found dead, her position upon the pillows being unchanged. This was fifteen hours after admission.

*Necropsy.*—An examination of the body, limited to the thoracic viscera, was performed seven hours post-mortem. The body was well developed and well nourished.

Fig. 4.—A photograph of the fresh specimen. Note peculiar color value of tumor, which was semitranslucent and yellowish.

Moderate pitting edema was present on the legs below the level of the knees. Rigor mortis was present to a very slight degree and post-mortem lividity was prominent over the back, thorax and neck. The lips and ears were very cyanotic.

When the sternum and adjacent ribs were removed the left pleural cavity was found to contain 700 c.c. of clear straw-colored fluid. The right pleural cavity was entirely obliterated by dense fibrous adhesions between the visceral and parietal pleurae. The heart was displaced slightly to the left.

The pericardial cavity contained about 20 c.c. of clear straw-colored liquid. There was, however, a purplish hemorrhagic discoloration beneath the epicardium over the right auricle, obviously due to slight extravasation of blood. The pulmonary arteries opened in situ were entirely normal. The heart, after removal and freeing of blood clots, weighed 325 grams. The valve measurements were all within normal limits, T.V. 11 cm.; M.V. 10 cm.; P.V. 6.5 cm. The aortic valve was not opened as it showed no abnormality when examined from above or below. Examination of the various segments of all of the valves showed no evidence of vegetations, and there

was no thickening or scarring to suggest previous valvular injury. The myocardium of the left ventricle measured 11 mm. in thickness, and the right ventricle, which was somewhat hypertrophied, measured 5 mm. in thickness. There was no evidence of gross scarring in the myocardium on various section planes and all of the chambers were free of thrombi. On opening the left auricle, a tumor mass was found almost filling the otherwise empty cavity. This tumor consisted of a lobulated, poly-

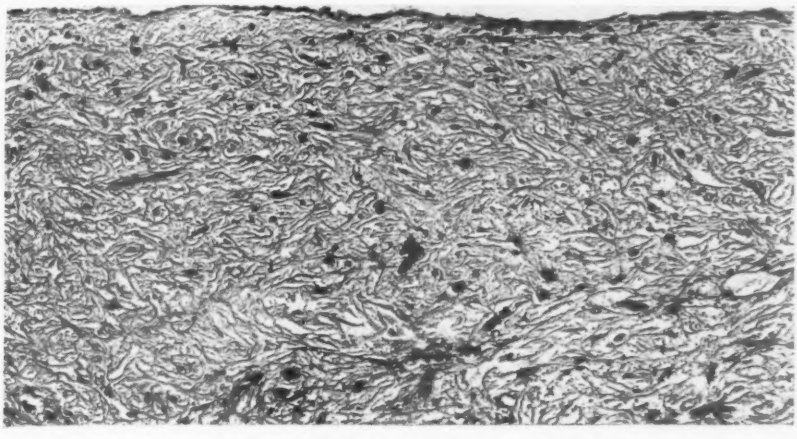


Fig. 5.—A low power photomicrograph showing a cellular border of the tumor, a fibrillary and granular matrix, fusiform and stellate cells and the elastic tissue fibrils. (Section stained with anilin blue.)

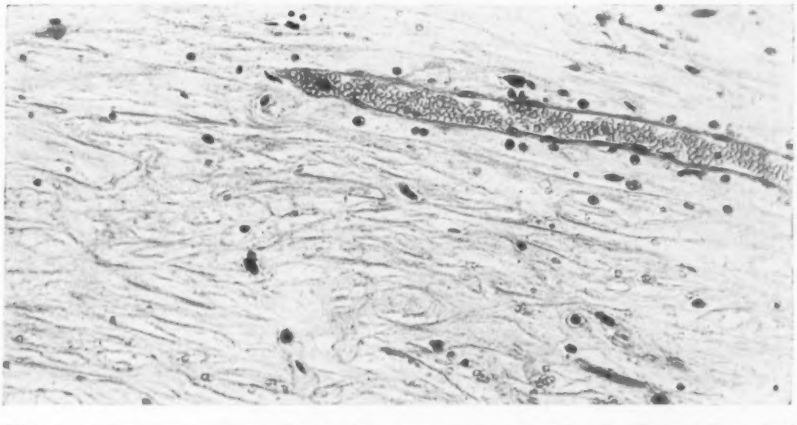


Fig. 6.—A low power photomicrograph showing the scarcity of cells and the relative abundance of pale staining intercellular substance. (Section stained with hematoxylin and eosin.)

poid growth, the external surface of which was smooth and glistening. In color it was pale yellow and on the fresh cut surface was soft, translucent and gelatinous. The only attachment to the auricular wall was by way of a dense fibrous pedicle measuring 5 mm. in diameter, which was firmly attached to the interauricular septum 11 mm. above the free margin of the mitral valve and about 8 mm. below a small perforate foramen ovale. The surface made by an incision through the interauricular septum from the right auricle showed the fibrous tissue of the pedicle to extend through one-half the diameter of the septum and to spread upward and downward in a fan-shaped manner.

The tumor measured 4.5 cm. by 4 cm. by 3 cm. in its greatest dimensions. When first seen, the polypoid growth rested snugly in the mitral valve, but it could be moved freely upon its pedicle and could be displaced well above the base of the valve segments. While fresh, the tumor appeared edematous; it was soft and jelly-like. Small snippings of the tumor when placed on a glass slide and examined microscopically were found to contain oval, fusiform and stellate connective tissue cells, in an abundance of transparent intercellular material. There were no areas in the gross to suggest thrombus formation.

*Microscopic Examination of the Tumor.*—Sections from the various portions of the tumor were stained by the following methods: eosin methylene blue, muci-carmine, phosphotungstic acid haematoxylin (Mallory), elastic tissue (Weigert), anilin blue (Mallory) and by Levaditi's method for the demonstration of spirochetes.

Paraffin sections stained with eosin methylene blue revealed a tumor which was poor in cells. The intercellular matrix or background in these preparations was uniform, stained faintly and was traversed by a fair number of thin-walled, small blood vessels and a few capillaries. In the anilin-blue preparations the background was resolved into blue-staining fibrils between which a finely granular, reddish brown material was incorporated. The phosphotungstic acid haematoxylin stain brought out the same type of intercellular material as a light brown, granular substance between more definite red brown, collagen fibrils. Occasional wavy elastic fibrils were seen in the sections stained by Weigert's elastic tissue method. None of the sections stained by appropriate methods gave typical mucin reactions. In general, the cells were elongated and fusiform in shape, though there were branching and stellate forms like those of embryonic connective tissue. The cells of the tumor were arranged either singly or in small groups and cords of from two to six cells each. In many instances there were small cell clusters about which a condensation of collagen had occurred. Excepting the fusiform and branching forms, the majority of cells were small, oval or round with a scant rim of cytoplasm surrounding a prominent and good sized nucleus.

No definite architectural detail could be made out except at the very periphery where the collagen was very dense with fibrils running parallel to the surface. The surface of the tissue was covered in part by flattened or oval cells, entirely similar to those cells found in the substance of the tumor. Occasional fusiform or stellate shaped surface cells showed cytoplasmic extensions into the underlying intercellular matrix.

Sections from near the tumor pedicle showed a small area, 4 mm. in diameter, in which there were numerous phagocytic cells, laden with hemosiderin granules. No other such areas were found in sections from other portions of the tumor. In the pedicle of the tumor there was marked condensation of the collagen into dense interlacing bundles. Examination of sections from representative blocks stained by Leviditi's method for the demonstration of spirochetes proved entirely negative.

## DISCUSSION

A few authors, notably Warthin,[7] have felt that cardiac myxomas were not true neoplasms but that in reality they represented degenerating forms of organized thrombi. Warthin found intramural mucoid nodules of the heart in congenital syphilis, the nodules of which resembled mucoid tissue and gave positive mucin reactions. In these myocardial lesions he was able to demonstrate colonization of Spirocheta pallida. These lesions, together with the finding of mucous-like connective tissue in organizing thrombi and in the early stages of organizing valvular vegetations, caused him to conclude that the entire group of reported cardiac myxomata should be rejected as myxoblastomas.

Wells,[8] on the other hand, has felt that many of the so-called myxomas are in reality edematous fibromas or polypoid tumors, in which the resemblance to true myxoma is more structural than chemical. He further states that this form of mucoid degeneration seems to be a reversion to the fetal type of connective tissue, which is characterized, as in the umbilical cord, by an excessive accumulation of a mucin-containing fluid intercellular substance and a paucity of collagenous fibrils.

We have had no hesitancy from the first in considering the present specimen as a true tumor composed of a fetal type of connective tissue and hence myxomatous in appearance. We also have concluded that many of the reported cases were so remarkably similar that they also should be placed among the true connective tissue tumors. The present tumor was found attached to and embedded in the wall of the left auricle by a dense connective tissue pedicle. The surrounding endocardium as well as the lining of all the chambers of the heart showed no evidence of scarring or active inflammation, and there were no thrombi. We have found no reports of single vegetations or solitary thrombi arising from the interauricular septum, in otherwise normal hearts. Norton[9] found that according to reported cases, 75 per cent of the so-called cardiac myxomas occurred in the left auricle. Granting that organizing thrombi and vegetations with early organization may show embryonic or mucous connective tissue, there should be portions of these large tumors which would show remnants of the original thrombus. Scattered groups of hemosiderin-filled phagocytes would not be conclusive evidence of thrombus origin, since small focal hemorrhages in pedunculated tumors would be likely to occur subsequent to minor strangulation or tortions. A thrombus would be expected to show evidence of layer formation and to be more dense in the central portion. The present tumor was uniform throughout, being pale yellow, translucent and gelatinous. It should also be emphasized that it had a smooth, though lobulated, and glistening external surface with no attached blood clot. Histologically the cellular elements were mostly those of embryonic connective tissue, the intercellular substance was mucinous in structure, elastic fibrils were numerous, and there were a fair number of orderly arranged blood vessels. Ewing[10] states that primary sarcomas of the heart are probably connected in origin with the myxomas. He also refers to the possible origin of myxomas in the superfluous embryonal tissue in the region of the foramen ovale, where so many of these growths have been attached.

In view of the pathological findings, an analysis of the mechanism producing the presenting symptoms is of interest. The rapid onset of symptoms in an adult, who has always been well, would necessitate either a rapid enlargement of the tumor or some alteration in position to produce the signs of valvular disease. Rapid enlargement of a tumor of this type could occur through edema or hemorrhage, the latter changes resulting from partial or complete obstruction of the blood vessels of

the pedicle by torsion. With the enlargement of the tumor, the auricular cavity would be taken up by the neoplasm so that insufficient space would be available for proper circulatory function. Valvular stenosis and insufficiency are possible when, as in this case, the tumor arises from a valve segment or when the pedicle is sufficiently long to allow the growth to project into the valve orifice. Pavlowsky[11] observed in the case reported by him that when the patient was lying down, there were signs of mitral insufficiency; when in a sitting posture there were signs of mitral stenosis, with much greater distress to the patient. These relationships were confirmed by similar positions at necropsy.

Our informant denied the occurrence of any convulsive or epileptiform movements, although such seizures are probably the most frequent presenting symptom in this type of cardiac tumor. A striking feature of the history, however, was the occurrence of five sudden attacks of fainting. Each of these attacks occurred while the patient was in the standing position. It seems possible that the fainting could have been caused by the pedunculated tumor dropping into and partially or completely blocking the mitral orifice. The subsequent fall to the horizontal position may have dislodged it. We feel with Weltmann[12] that the above mechanism may at times suggest the Adams-Stokes syndrome.

## SUMMARY

1. A case of intracardiac tumor arising from the interauricular septum is reported and illustrated by gross and microscopic photographs.

2. We have found no record of this condition ever having been diagnosed before necropsy.

3. A tumor of this type may produce a ball-valve action in every way similar to the action of a ball thrombus.

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# ANEURYSMS OF THE BRONCHIAL ARTERIES*

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ANEURYSMS have been described in many arteries. They have been found involving nearly every part of the arterial system from the sinus of Valsalva to the smaller peripheral arteries of the brain, abdominal viscera, and the extremities. A careful search of the literature fails to disclose any reference to aneurysm formation of the bronchial arteries, a case of which came to my attention at the Harlem Hospital.

These arteries, one right and two left, usually arise from the anterior wall of the thoracic aorta just above the level of origin of the intercostal arteries. Frequently the right and occasionally the left arteries arise from the upper aortic intercostal arteries as small branches of these vessels or by a common stem. In the case reported, these vessels arose directly from the aorta, in line with the intercostal arteries. There were twelve such pairs, all arising from the posterior aortic wall; from the anterior wall, no branches arose. The lower nine pairs of arteries were distributed to the intercostal spaces; the upper three ran in the direction of the bronchi.

## CASE REPORT

J. C., aged thirty-five years, colored male, was admitted to the Harlem Hospital, in a semistuporous condition. The meager history obtained from his brother was that he had apparently been well until two days before admission when he developed an unproductive cough and experienced difficulty in breathing. Patient had difficulty both on inspiration and expiration, his breathing being of a "crowing" nature. The cough and dyspnea became more severe. On the day of admission he seemed dazed, his speech incoherent. No other symptoms were present, nor did his brother think there had been any fever.

While in the admitting room (where he had been sent by his physician as a diphtheria suspect) he suddenly became very cyanotic and lapsed into coma. Tracheotomy was performed, a tube inserted into the trachea in the midline immediately below the larynx, without relief of his symptoms.

Physical examination (in the ward) disclosed a well-developed and nourished young colored adult male, breathing in a very labored manner. Skin was cold, rather clammy. Corneal reflexes were active; pupils in mid-dilatation, equal, and reacting sluggishly to light. Ears, nose and mouth were negative. Tracheotomy tube was present in the midline of the trachea, below the larynx. Heart seemed pushed to the right, the right border being in the midclavicular line, the left border at the left sternal border. The cardiac dullness area in the first interspace meas-

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ured 4 inches in width, equally to the right and left of the midline. Heart sounds were faint and distant but were heard throughout the entire anterior chest; no murmurs; $A_2$ accentuated.

Lungs showed no impairment of resonance. Breath sounds were faint and distant; no râles present. Suprasternal and substernal retraction of chest marked.

Abdomen, extremities and reflexes were negative.

Blood pressure on the two arms showed systolic 90 mm., diastolic 50 mm. on the right, and systolic 106 mm., diastolic 60 mm. on the left.

Fig. 1.—Anterior view of heart and aorta showing openings of aneurysms in line of lateral intercostal arteries, and displacement of left subclavian and carotid arteries to right.

*1*, Left common carotid; *2*, *3*, *4*, openings of aneurysms.

Temperature on admission 100°; pulse 76 and regular, unequal, right stronger than left; respirations 20, shallow and very labored. Four hours later (just preagonal) temperature was 100.2°; pulse 96; respirations 32.

Blood count showed R.B.C. 3,800,000; Hgb. 70 per cent (Sahli); W.B.C. 13,000; polynuclears 77 per cent; lymphocytes 21 per cent; transitionals 2 per cent.

Urine showed a trace of albumin, a few hyaline and granular casts, and an occasional erythrocyte.

The coma deepened, the obstructive breathing became more labored and shallower. Generalized twitches of the entire body appeared. Death supervened four hours after admission.

AUTOPSY REPORT

Body is that of a well-developed and nourished young male negro, 68 inches in length. Two-inch midline tracheotomy incision beginning immediately beneath lower border of thyroid cartilage.

Neck organs not grossly remarkable.

Chest: On opening the chest, a large mass rises from above the first portion of the descending aorta, just beyond the left subclavian artery, and projects upward to the superior aperture of the chest. The left subclavian artery is pushed to the right; its lumen narrowed, measuring 0.5 cm. at its origin and for 2.5 cm. of its

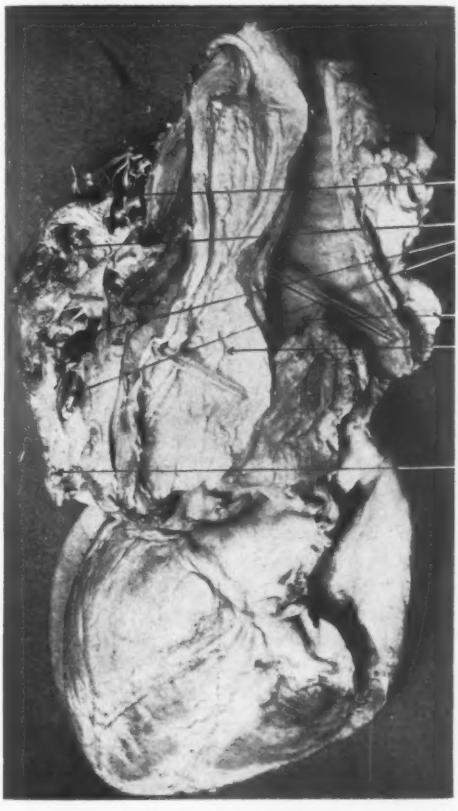


Fig. 2.—Posterior view of aneurysmal mass to show relation to trachea, left bronchus, and esophagus (held by glass rods) and posterior view of aneurysmal openings.

*1*, Upper end of mass; *2*, *3*, *4*, openings of aneurysms (filled with blood clot); *5*, left main bronchus; *6*, esophagus; *7*, lower end of mass.

course, where it winds anteriorly to and above the mass in its course to the axilla, its lumen then widening to 1.2 cm. The mass measures 6 x 10 x 5 cm. It extends downward along and behind the descending thoracic aorta to the level of the fourth intercostal arteries. Posteriorly it extends behind the aorta, left subclavian and left common carotid arteries. It compresses the esophagus and trachea, completely occluding the esophagus and left stem bronchus at its origin. At the bifurcation, the tracheal lumen is very markedly narrowed, barely admitting a probe 0.2 cm. in diameter.

The outer upper surface of this mass is intact, very thin; beneath it a firm blood clot is visible. The posterior surface was torn across in removing the speci-

men. It presents three distinct openings respectively from above downward 3, 2, and 1 cm. in diameter, filled with clotted blood. These openings are separated from each other by narrow bands of tissue continuous with the surface covering.

On opening the aorta, in the line of the lateral intercostal arterial mouths, are three large openings, respectively 1, 2, and 0.6 cm. in diameter from above downward. Corresponding to these openings are three minute openings in the line of the medial intercostal arterial mouths. The large openings lead directly into the blood-clot-filled mass described. When the clots are evacuated, the mass appears as three wide noncommunicating tubes, each about 4 cm. in length. The wall of each is thin, the inner surface eroded and without any intima. The wall of the aorta at the site of the openings and in various portions of the ascending arch and descending aorta measures uniformly 0.4 cm. in thickness; that of the tubes is paper thin. Its wall is directly continuous with the aortic wall. The course of the lower nine intercostal arteries can be traced from their origin well under the ribs; that of the first three lateral arteries is lost in the mass, being demonstrable for only a short distance near the esophagus and left bronchus.

The intima of the aorta contains numerous small yellowish atheromatous plaques and innumerable fine longitudinal striations. Around these striations the intima is of a light brown color. The aorta is quite inelastic. The striations are most numerous in the sinuses of Valsalva and in the arch and descending aorta near and between the large openings described, where the intima is markedly puckered.

The heart is relatively small, weighs 165 gm. Pericardium smooth, glistening; no fluid present in sac. Myocardium firm, not thickened; papillary muscles not thickened, chordae tendineae not shortened. Aortic valve cusps definitely thickened along line of attachment where a few small atheromata are present; remainder of valve and other valve cusps are thin and translucent. Aortic cusps were retracted from coronary arteries.

MEASUREMENTS

| | |
|---|---|
| Thickness left ventricle | 2.0 cm. |
| Thickness right ventricle | 0.4 cm. |
| Circumference aortic valve | 6.0 cm. |
| Circumference mitral valve | 7.2 cm. |
| Circumference pulmonary valve | 8.0 cm. |
| Circumference tricuspid valve | 11.2 cm. |

All the pulmonary lobes were markedly emphysematous, collapsing somewhat when the heart and mass were removed. Abdominal organs not noteworthy.

MICROSCOPIC EXAMINATION

1. Sections of the arch and descending portion of aorta showed marked lymphocytic and plasma-celled perivascular infiltration of the vasa vasorum and fragmentation of the medial elastic tissue fibers. The intima showed some endothelial proliferation and numerous collections of needle-like cholesterin crystals in the subendothelial tissue. The inner elastic lamella was intact.

2. Sections of the wall of the aneurysmal sacs showed the intimal lining present in but a few places; the inner elastic lamella and the medial elastic tissue are markedly fragmented, numerous very short, frayed fragments being apparent in the fibromuscular tissue of the wall which is rather densely infiltrated with lymphocytes. A few small arterioles, near the outer edge of the wall, show a marked perivascular zone of lymphocytes. No spirochetes demonstrable (Levaditi stain).

3. Sections of the first four intercostal arteries and proximal three centimeters of innominate, left carotid and subclavian arteries showed a picture similar to that

in the aorta. Sections of other portions of the carotid arteries, the iliacs, and proximal two centimeters of the hepatic and superior mesenteric arteries showed a slight perivascular lymphocytic infiltration of the vasa vasorum; no elastic fiber fragmentation was present. A few of these vasa vasorum showed marked proliferation of the intima and narrowing of the arterial lumen. No hyalinization or calcification of the wall, nor thrombi in the lumen, or ulceration of the intimal surface was present. The other vessels showed the intimal proliferation to a less marked degree.

Sections of other arteries (renals, splenic, inferior mesenteric, pulmonary) showed an occasional adventitial vas vasorum surrounded by a narrow, usually single-celled, layer of lymphocytes. In these sections an occasional vas vasorum showed a slight degree of intimal proliferation.

4. Sections of the heart (interventricular septum, near base, and right and left ventricular walls) show small areas of fibrous tissue irregularly distributed between the muscle fibers, fading indefinably into the finer intermuscular reticular tissue, and only here and there apparently close to a blood vessel. The intima of the larger arterioles is moderately proliferated; no cellular infiltration of the wall is present.

5. Sections of the other organs show no noteworthy changes.

## DISCUSSION

Aneurysms of the smaller arteries have been described in the brain,[1] coronary,[2] hepatic,[3] renal,[4] gluteal,[5] popliteal and posterior tibial[6] arteries. These are seldom of syphylitic origin. Thus the very infrequent renal arterial aneurysmal dilatations described were multiple, generally at the hilus or in the adjacent parenchyma, and varied from the size of a walnut to that of a child's head. They were generally caused by perivascular (intraperitoneal) inflammatory lesions;[7] tuberculosis[3] and atherosclerosis and trauma[8] have also been reported as etiologic factors.

Syphilis as a cause of aneurysms of the smaller arteries seems rather infrequently mentioned. In fact, even in the aorta, luetic aneurysms appear hardly more frequently than aneurysms of arteriosclerotic nonluetic origin. According to Berger,[1] even at the base of the brain where the smaller arteries more frequently present aneurysms than elsewhere among arteries of similar size, not more than 10 per cent are syphilitic in origin.

In the case reported the luetic basis of the aneurysms was unquestioned, on histologic grounds. It is furthermore interesting to note the extensive mesaortitis of other smaller arteries not showing aneurysms. This rather extensive involvement of the medium-sized arteries was very recently stressed by Saphir[9] who, in a study of fifty cases of syphilitic aortitis, found syphilitic changes in the innominate artery in thirty-three cases, in the carotid in twenty-nine, in the superior mesenteric and common iliacs in ten, in the inferior mesenteric in three and the femoral artery in seven cases. The early changes observed by him were characterized by an endarteritis of the vasa vasorum and a perivascular infiltration of lymphocytes in the adventitia. These early histologic evidences of syphilitic involvement occurred in our case in

the distal portions of the common carotid and common iliac arteries and the proximal 2 cm. of the hepatic and superior mesenteric arteries. In the renal, splenic, inferior mesenteric and pulmonary arteries similar involvement of the vasa vasorum and adventitia was present but to a far lesser extent. In the innominate, proximal part of the left common carotid and the left subclavian arteries evidence of a more advanced process was present in the form of fragmentation of the elastic fibers and interruption of the elastic lamellae. These latter changes were also apparent in the wall of the aorta, of the aneurysmal sac, and the first four intercostal arteries.

It appears that this was a case in which a very extensive syphilitic involvement of the arteries of all three sizes had occurred. The lesions were most pronounced and of longest duration in the arteries of the first and some of the third magnitude (bronchial and intercostal arteries). It appears not unlikely that those of the latter category not having a bony or surrounding muscular protective wall—the first three intercostal arteries, the bronchial arteries—formed aneurysms; these sacs in turn, by their external pressure perhaps preventing similar aneurysmal formation from the thicker walled aorta. The other intercostal arteries, although apparently as markedly involved in the syphilitic process but surrounded by firm supporting structures, did not form aneurysms.

## SUMMARY

1. A case of multiple, saccular aneurysms of the bronchial arteries is reported, the first recorded in the literature. Death resulted from asphyxia caused by tracheal occlusion by the aneurysm.

2. The etiology is shown definitely to be luetic, a rather unusual finding in aneurysms of smaller arteries. Many other small and several medium-sized arteries showed syphilitic involvement varying from the early lesions of endarteritis of the vasa vasorum and lymphocytic perivascular infiltration of the adventitia to extensive destruction of the elastic lamellae.

3. The rôle of the supporting external structures in the formation of the aneurysms of the intercostal arteries and aorta in this case is indicated.

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# Department of Clinical Reports

## "PLATEAU R-T" IN A CASE OF LOBAR PNEUMONIA*

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DURING the past ten years, a good deal has been said regarding an electrocardiogram which is characteristic of coronary artery disease. Rothschild, Mann and Oppenheimer,[1] Pardee,[2, 3] and Parkinson and Bedford[4] have all described a change which appears soon after the occurrence of coronary occlusion as well as the so-called "coronary T-wave" or "cove-plane T" which develops several days after such an accident. It is this first change in the ventricular complex in which we are particularly interested at present. This is designated by Parkinson and Bedford as the pleateau R-T and is universally described as a take-off of the T-wave from a point near the top of the R-wave on its downward limb. All of the above-named authors agree that this type of curve is characteristic of the early stages of coronary thrombosis.

This same type of electrocardiogram has been found in several other conditions: Kountz and Gruber[5] obtained it experimentally by producing anoxemia. They saw it in moderate degree after general anoxemia and after vago-pression. Scott, Feil, and Katz[6] reported it in cases of pericardial effusion which had come to autopsy and were known to have no coronary artery disease. De Graff and Wible[7] reported it after digitalis.

The present case is one of lobar pneumonia in which this plateau R-T was found during the routine examination of daily electrocardiograms taken as a part of the work on the study of digitalis in pneumonia.

The patient was a Mexican boy of twenty-two years who had been perfectly well until the acute onset of his present illness. Three days before entry he had a chill followed by fever, pain in the right upper chest, and cough with production of reddish brown sputum. He remained in bed most of the time before coming to the hospital and had no treatment other than cupping.

The family history was irrelevant, and the past history negative. His habits were good.

On entry, January 22, 1930, he was moderately cyanotic and dyspneic. The heart was not enlarged, the rate was regular, the sounds of good quality, and there were no murmurs. The blood pressure was 110/70 mm. In the right upper lobe

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anteriorly and posteriorly, the percussion note was dull, the breath sounds were bronchial with many crepitant râles, and the voice sounds were increased. Anteriorly, there was a definite pleural friction rub. Otherwise the lungs were clear. The diagnosis of pneumonia of the right upper lobe was substantiated by fluoroscopic examination.

The lung findings remained practically the same until January 31, when definite signs of resolution were noted. By February 3, these had disappeared and the lungs were entirely clear. The heart was examined daily and at all times the sounds were clear and of good quality. Never was a pericardial friction rub heard and never were any abnormal pulsations seen. The patient never admitted having any pain besides that in the right upper chest. Cyanosis was moderate at the time he entered and gradually decreased until January 27, when it was no longer noted. There was moderate dyspnea on admission but this had disappeared by the end of the fourth day, which was the fourth day before the temperature had dropped. There was no great prostration during the acute stage and there was less weakness following the illness than is usually found after pneumonia. The blood pressure

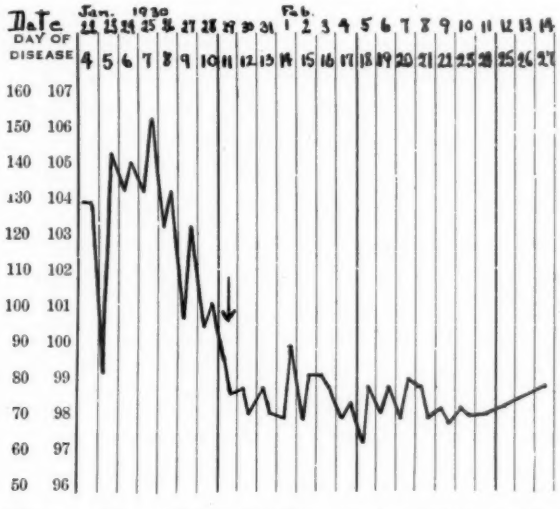


Fig. 1.—Temperature Chart. Arrow indicates date on which plateau T-wave first appeared. Note that the temperature curve at this time is dropping very rapidly.

was taken at short intervals and remained approximately the same as on admission. The urine was negative except for a trace of albumin. The sputum contained pneumococci type V. and the patient was treated during the febrile period with antipneumococcus serum mixed: types IV. V. and XIII.[8] At no time did he receive digitalis.

On the 11th of February, the patient was discharged in good condition. On the 14th, he returned for the customary reëxamination when there were no abnormal physical findings. On the same day, he was given an exercise tolerance test according to the method of Master and Oppenheimer[9] which gave him a rating of 26, the normal for his age, weight, height and sex, being 25.

The electrocardiographic findings are shown in the accompanying figures. It will be noted that although the point of origin of the T-wave on the R-wave began to rise during the febrile period, it reached its greatest height on January 29, when the temperature had dropped to 98.8 degrees. Since the temperature was normal when the T-wave showed the most marked plateau form, and since the cyanosis had disappeared even before this, we feel that the picture cannot be explained by

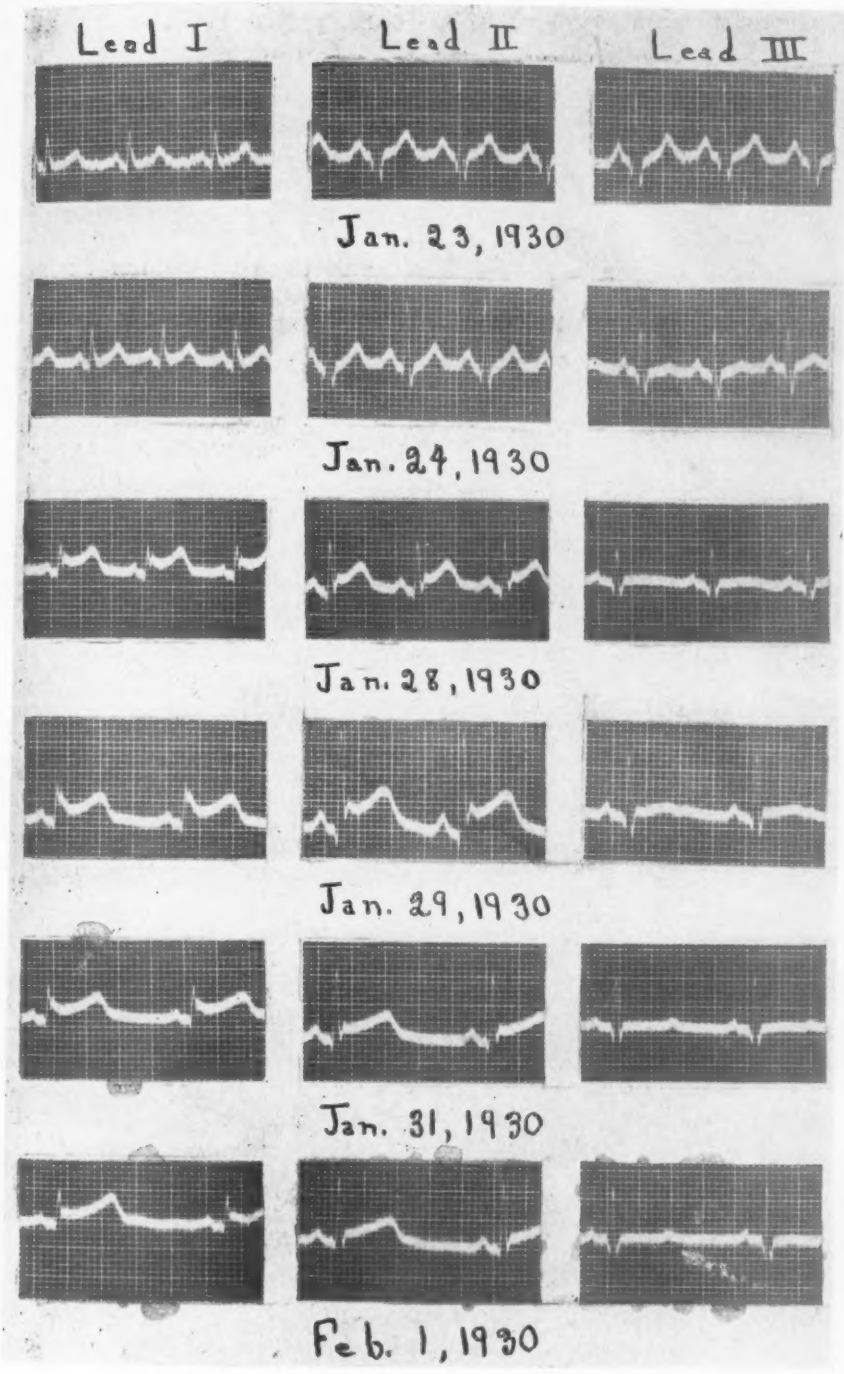


Fig. 24.—Successive changes in the electrocardiogram.

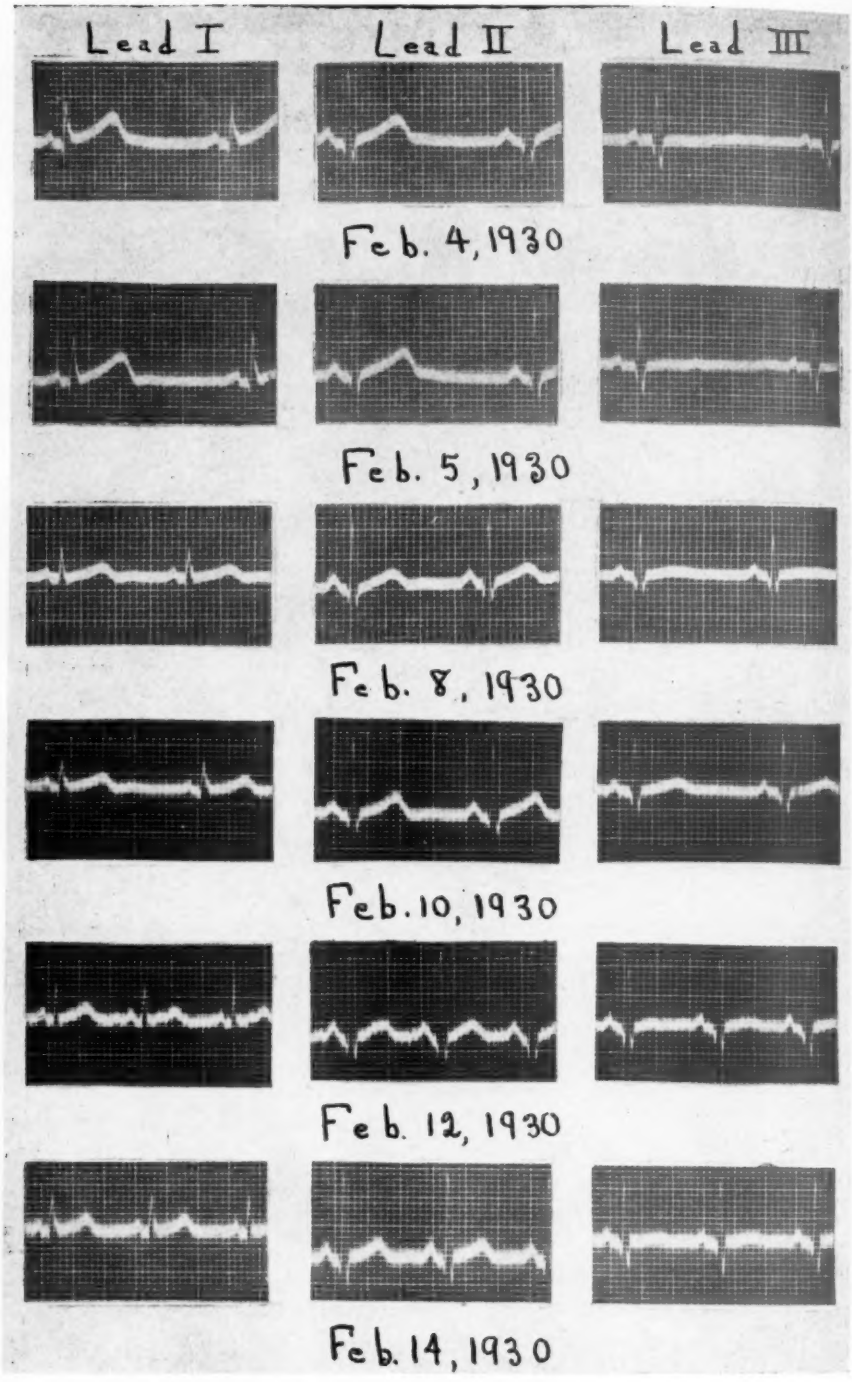


Fig. 2*B*.—Successive changes in the electrocardiogram.

anoxemia. It will also be seen that the S-T segment gradually returned to normal rather than developing into the phase of the cove-plane T. This transition, therefore, is different from that usually described as occurring during the course of coronary thrombosis. In view of this fact as well as that the patient recovered without any functional impairment of the heart, we are convinced that the S-T segment of these electrocardiograms must have some cause other than coronary artery disease, pericarditis, anoxemia, or digitalis. At the present time the exact cause is still in doubt. A possible explanation is toxic myocarditis, but there was nothing in the clinical picture to substantiate this.

SUMMARY

A case of lobar pneumonia is reported in which the electrocardiograms show a "plateau" or "high take-off" type of T-wave without clinical evidence of coronary artery disease.

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# Department of Reviews and Abstracts

## Selected Abstracts

**Van Liere, E. J., and Crisler, George: The Influence of the Pericardium on Acute Cardiac Dilatation Produced by Vaginal Stimulation.** Am. J. Physiol. 94: 162, 1930.

In continuation of work done previously by the authors, a study has been made of the restraining influence which the pericardium might exert on the heart. Instead of anoxemia as used in the previous experiments, the authors used vagal stimulation to produce the acute cardiac dilatation. The extent of the cardiac dilatation was measured by x-ray plates. Dogs were used in the experiments. It was observed that animals with the pericardium incised showed a greater cardiac dilatation when the vagus was stimulated to cause cardiac standstill than do animals with the pericardium intact. In some of the animals the evidence of dilatation was slight, but in all the tendency was for the heart to become dilated. In animals without pericardiotomy there was no appreciable change following vagus stimulation.

The authors believe that the pericardium restrains excessive cardiac dilatation caused by vagal stimulation and that this is further evidence that the pericardium exerts a protective action on the heart in conditions of extreme stress.

**Weese, H.: I. Digitalis Consumption and Digitalis Effect in Warmblooded Animals.** Arch. f. exper. Path. u. Pharmakol. 135: 228, 1928.

A few minutes after the intravenous injection of digitalis, the greater part of the digitalis has disappeared. It has not been known what happens to it. No digitalis is found in defibrinated blood. It is not excreted in the intestine and urine. The purpose of the investigation was to show where the digitalis was stored and destroyed. This was done on Starling's heart-lung preparation on cats. The preparation was perfused with cat's blood, in some cases diluted with Tyrode solution, against an arterial resistance of 80 to 100 mm. Hg. The venous pressure was 8 to 10 cm. Water temperature was 38° C. The glucosides which were tested were digitoxin, G. Strophanthin scillaren. The criterion of the digitalis effect was asystole of the heart.

THERAPEUTIC EFFECT

The effect of the digitalis glucosides on the damaged heart varied considerably during the therapeutic stage depending upon the extent of the damage. This applied both to amplitude and minute volume. In preparations working under optimal conditions there was no therapeutic effect.

TOXIC EFFECT

With high concentration and rapid effect the amplitudes decreased gradually; the frequency remained constant and rhythm regular. Auricular and ventricular fibrillation then followed, and the heart then stopped, mostly in diastole.

In slow poisoning intermittent irritation and conduction disturbances occurred. Cushny's periodic variations were observed. Then followed intermittent flutter and fibrillation ending in death.

THE GLUCOSIDE CONSUMPTION OF THE HEART

Of the heart, lungs, and blood, the heart only showed a measurable affinity for the digitalis. It was found that the minimal lethal dose per gram heart was as follows:

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|---|---|
| Digitoxin | 0.0046 |
| G. Strophanthin | 0.0020 |
| Scillaren | 0.0022 |

From experiments on the entire animal it was found that 9 per cent of the injected strophanthin was bound to the heart, 4.5 per cent of the scillaren. The digitoxin percentage lay between the two. The absolute effect on the isolated cat's heart was the same for G. Strophanthin and scillaren. For digitoxin it was only half that.

The next problem was, how much of the glucosides present in the blood did the heart absorb? It was found that when the calculated minimal lethal dose was present all the glucoside was taken up by the heart. If there was any more in the perfusion fluid at the beginning of the experiment, the surplus was still present at the end. The functional state of the heart did not influence the minimal lethal dose. Conclusion: For the warm-blooded animal the minimal lethal dose is also the absorption dose or effective dose. The dose is independent of the concentration of the glucoside.

From the literature it appears that the frog heart in room temperature can only be brought to asystole when one c.c. of the perfusion Ringer contains many times the consummation dose. Consequently a frog heart cannot completely remove the digitalis from a perfusion fluid. This is not true at lower temperatures. Conclusions: The heart muscle of all vertebrates is able to store digitalis glucosides.

The scillaren which was bound in the heart or which was present in blood (blood sample in ice chest) spontaneously disappeared. Digitoxin and strophanthin are not destroyed by the blood. The rate of action of digitalis glucosides is a direct function of the concentration.

**Weese, H.: II. Digitalis Consumption and Digitalis Effect in Warmblooded Animals.** Arch. f. exper. Path. u. Pharmakol. **141:** 329, 1929.

In this paper the author traces the fate of the digitalis glucosides which were not bound by the heart.

Especially musculature, liver, and kidney tissue preparations were examined, and these were shunted into a heart-lung preparation.

Muscle was found to absorb glucosides up to a certain point. It did not let any glucosides pass until it was completely saturated. After that glucosides were allowed to pass with the perfusion fluid. The time required for fixation is short, probably seconds.

The digitalis consumption of the liver is somewhat irregular, probably depending upon the fat content of the organ. But it does bind considerable amounts of glucosides. The conditions of absorption are similar to those found in the muscles.

Muscle and liver absorbed far less digitalis than the heart. The kidney was the only organ which bound a comparable amount of glucoside. The lungs bind no glucosides. The amount of glucoside bound by the muscle is in the summer 10 to 14 times, in the winter 5 times less than that bound by the heart. But as they exceed 50 per cent of the body weight, they nevertheless bind the greater part of administered glucoside. In absolute figures the liver and kidney also bind more glucoside than the heart.

If the dose of glucosides, which corresponds to the minimal lethal dose when injected intravenously, is injected into the aorta, then no digitalis reaches the large

veins. It is all bound in the body. The ability of the body, outside the heart, to absorb digitalis is 1.7 times the minimal lethal dose. Therefore, with an intravenous minimal lethal dose the heart only is saturated with glucoside, not the remainder of the body.

The conclusion is that all digitalis glucoside which leaves the heart is bound peripherally in the body and will be of no more benefit to the heart.

Next the authors investigated the relation between the rapidity of injection and the minimal lethal dose. The premises were: The effective dose of digitalis is constant with constant temperature and constant heart weight. The healthy heart can only bind glucoside during the period of injection. Variations of intravenous minimal lethal dose depends upon variation in utilization of the glucoside contents of the blood.

Digitalis binding in the heart primarily is by reversible adsorption, secondarily follows an irreversible fixation. Therefore, adsorption surface and adsorption time are factors which determine the amount of glucoside taken up. More digitalis is bound with increasing concentration, with slower perfusion rate. If these are equal, more strophanthin than digitoxin will be found. The absorption rate, therefore, is quicker for the water soluble strophanthin. The time factor seems more important than the concentration factor.

DIGITALIS ABSORPTION IN THE INSUFFICIENT HEART

Insufficient hearts respond to digitalis with greater ease than compensated hearts. Also slow intravenous injection produces a better effect without toxic side effects, than does rapid injection of larger doses. The general explanation of this increased response is that a sensitization to digitalis exists in the decompensated heart. The author reasons that in cardiac hypertrophy and dilation there is an increased cardiac surface and increased area of coronary circulation; that is, an increased absorption surface. In decompensation the dilated heart is unable to drive the blood out during systole. This blood containing glucosides remains longer in contact with the ventricular wall than in a healthy heart. The same delay occurs in the coronaries. Therefore in decompensation both absorption surface and absorption time will be increased. This favors increased utilization of digitalis. Also, the slower the injection of digitalis, the greater the utilization.

STANDARDIZATION

The accuracy of the cat infusion method varies between better than 10 (De Lind van Wyngearden) and less than 27 per cent. Though the method is subject to some criticism, it is of some value which, however, does not exceed that of the frog preparation. The only proper way to standardize digitalis for parenteral administration is by perfusion under circumstances where the heart is the only organ absorbing the drug and then to give the minimal lethal dose.

**Weese, H.: III. On Digitalis Accumulation.** Arch. f. exper. Path. u. Pharmakol. **150:** 14, 1930.

Problem: Does the glucoside which has been found outside the heart have any cardiac effect after it has been bound?

Cloetta found that muscle binds digitalis irreversibly, after which ferments split it into aglycone and sugar. The aglycone is carried by the blood to the heart, where it exerts its specific action and leads to accumulation. The author showed, however, that the accumulation was not caused by digitalis found outside the heart, but by that found in the heart itself. Intact cats were given a sublethal dose of digitoxin. From two to twelve days later a heart-lung preparation was made from these cats, and it was found the actual lethal dose now was equal to the calculated lethal dose for a fresh heart of the same weight, minus the amount

bound by the heart after the injection into the intact animal. This amount, however, gradually disappeared at the rate of 3 to 4 per cent of the minimal lethal dose per day.

The conclusion is that only the digitalis bound in the heart contributes to accumulation, that bound in the tissues is worthless.

**Grollman, Arthur: The Action of Alcohol, Caffeine and Tobacco on the Cardiac Output (and Its Related Functions) of Normal Man.** J. Pharmacol. & Exper. Therap. **39**: 313, 1930.

The present paper presents data on the changes in the pulse rate, blood pressure, oxygen consumption, arteriovenous oxygen difference and cardiac output which follow the use of alcohol, caffeine, and tobacco. The determinations were all carried out on normal young adults under basal conditions. Pulse rate determinations were made by radial palpation for one minute. Blood pressure records were obtained with the Tycos recording sphygmomanometer. Oxygen consumptions were determined with the Krogh spirometer. The determinations of the cardiac output were made by the use of acetylene gas as described by the author.

The administration of even small doses of alcohol to nondrinkers resulted in a psychic response characterized by a transient rise in pulse rate, blood pressure, and cardiac output with a drop in the arteriovenous oxygen difference. Where no psychic reaction was elicited as in moderate drinkers such changes did not occur. In such cases amounts of alcohol equivalent to 60 c.c. of whiskey showed no demonstrable changes in blood pressure, oxygen consumption, arteriovenous oxygen difference, or cardiac output with a change of only a few beats per minute in the pulse rate during the first half hour after its administration. Larger quantities of alcohol caused slight changes in the pulse rate with appreciable increases in the blood pressure and cardiac output.

Small doses of caffeine were without effect on the cardiavascular system. Larger doses caused, in most cases, a rise in the oxygen consumption, slight or no changes in the pulse rate, an increase in the arteriovenous oxygen difference, and a slight rise in the cardiac output.

Tobacco, when indulged in its usual forms in moderate amounts by habitual smokers, produced no demonstrable changes in blood pressure or cardiac output with only slight or no increase in the pulse rate. Excessive smoking or smoking of tobacco in unaccustomed forms resulted in very large rises in blood pressure and moderate increases in cardiac output. When the blood pressure changes were slight, the cardiac output changes were minimal or absent.

**Marshall, E. K.: The Cardiac Output of Man.** Medicine **9**: 175, 1930.

In this Harvey Lecture, the author discusses briefly the various methods used at present in the determination of the output of the heart under experimental and clinical conditions. He describes principally the method developed by Grollman and himself. This consists of inhalation of acetylene gas, and the measurement of its absorption and distribution. He believes that the estimation of the cardiac output can be determined for normal individuals under the basal conditions with results as satisfactory as those derived from estimation of basal metabolism. Using the acetylene gas method, the error of determination in a series of 50 normal individuals was no more than plus or minus 0.3 liters per square meter of body surface.

The author believes that the position of the subject and posture is without considerable influence on the cardiac output, when basal conditions are established for the determination of the cardiac output. Determination of cardiac output following ingestion of food shows that there is marked increase directly proportionate to the amount of food eaten. He discusses the influence of emotional state

of the subject and of muscular exercise on the cardiac output. He believes that both these influences are very marked and produce extreme changes in cardiac output.

**Howell, W. H., and McDonald, C. H.: Note on the Effect of Repeated Intravascular Injections of Heparin.** Bull. Johns Hopkins Hosp. **46:** 365, 1930.

Results of this study indicate that a daily injection in dogs of a relatively large dose of purified heparin for six consecutive days does not cause any change in the corpuscles of the blood or any significant change in the clotting time. There was no indication of a shortening of this time but rather a slight tendency toward lengthening. It seemed that the excess of heparin injected into the blood was removed in part, at least, through the kidneys.

**Beneke, Rudolph: Factors Predisposing to Coronary Sclerosis.** Ztschr. f. Kreislaufforsch. **22:** 359, 1930.

The form and construction of blood vessels is determined by physical hydraulic processes. This holds true also of the construction of connective tissues. The direction of the fibers is determined by the direction of the pressure of the blood stream. In the vessels where the pressure is perpendicular on the axis of the vessel (e.g., the aorta) the connective tissue is arranged in rings. In vessels where the pressure is in the direction of the stream, the fibers run longitudinally (in the smaller arteries). The fibrous tissue of a valve of a vein runs longitudinally on the surface facing the blood current. Inside the pocket the direction is crosswise. It is concluded that every fiber of the body owes its direction to the pressure exerted upon it when it was formed.

Considering this principle in the blood vessels, it should be remembered that the blood current is made up of a number of partial currents exerting somewhat different pressures. The opinions of the origin of vascular degeneration are divided; some consider the lipoid changes in the intima primary, others consider medial degenerations primary. The author considers the two processes fundamentally different. They are both reactions to overstrain but occur from different causes. Sometimes the causes creating both act together and result in combined atherosclerosis. No sharp border can be drawn between the extents of the two processes, or between the physiological and the pathological wear and tear reaction. The lipoid intimal changes are produced by the lipoids of the blood which are precipitated out of the blood and pressed into the intima; this process is determined by the direction and the power of the blood current and by the vitality of the tissues. It is also determined by fibrosis of the underlying media and perhaps by toxic sensitization (nicotine infections?). Especially nicotine seems important for the development of coronary sclerosis, which is supposed to be common in smokers.

The intimal degeneration, however, is determined by a primary fibrosis of the media. This fibrosis is caused by the strain by the separate currents in the blood stream. These currents are determined as to direction and power by the forms of the vessels. The coronaries being naturally tortuous will create eddies which will strain their walls. This strain will be aggravated where the pressure is high as in hypertension. The mechanism of these currents is discussed somewhat in detail.

**Alt, Howard L., Walker, George L., and Smith, W. Carter: The Cardiac Output in Heart Disease. II. Effect of Exercise on the Circulation in Patients with Chronic Rheumatic Valvular Disease, Subacute Rheumatic Fever and Complete Heart-Block.** Arch. Int. Med. **45:** 958, 1930.

Four normal subjects and seven patients with compensated heart disease were subjected to two moderate standardized grades of work on the Krogh bicycle

ergometer. Measurements were made of the cardiac output, pulse rate, blood pressure during exercise. The response of the cardiac output in the patients with heart disease was not essentially different from the response of normal subjects. The lowest values occurred in a youth in good physical training with mild valvular disease who performed the work with ease and in a young adult with complete heart-block, who performed the work with difficulty.

Four of the patients with heart disease experienced fatigue and dyspnea during exercise. Fatigue was usually more marked than dyspnea. The first patient had advanced aortic and mitral disease with marked cardiac enlargement. The pulse pressure which was abnormally high at rest increased relatively as in the normal subjects during exercise. The second patient, who had subacute rheumatic fever, had an abnormal increase in the pulse rate while the stroke volume did not rise above its basal level. In the third, a young woman with complete heart-block, the pulse rate doubled during exercise. This was effected both by an increase in the ventricular rate and by the occurrence of extrasystoles. The fourth patient, a young man with complete heart-block, had a slight decrease in the pulse rate during exercise. This was accompanied by a greatly increased stroke volume, higher than any previously reported in the literature. Both patients with complete heart-block had an unusual rise in the pulse pressure during work.

**Sutton, D. C., and Lueth, Harold C.: Experimental Production of Pain on Excitation of the Heart and Great Vessels.** Arch. Int. Med. **45**: 827, 1930.

Symptoms analogous to these occurring in man in angina pectoris and coronary occlusion can be produced experimentally in the dog; namely pain, sometimes nausea and vomiting, stimultion of respiration and fall in blood pressure. By utilizing a method previously described for temporary occlusion of the coronary vessels in the unanesthetized dog and also methods for the production of pain and its transmission, the authors have found that compression of the artery, vein, and included tissue produces first a cyanosis of that portion of the ventricle supplied by the vessels; the vein becomes distended, while the myocardium becomes definitely paler. Almost immediately there is a definite and at times a marked increase in the volume of both ventricles, and later also of the auricles. Immediately following partial compression of the vessels there is a definite rapid fall in blood pressure, amounting to from 30 to 55 mm. of mercury. Marked irregularities of the heart appear and seem to be increased by anoxemia.

It is suggested that sudden death in angina pectoris may be the result of ventricular fibrillation occurring during temporary decrease in coronary flow.

Acute mechanical distention of the aortic arch, ascending aorta and aortic ring, and the cavity of the left ventricle does not produce pain in the dog. It does produce paroxysmal dyspnea. There may be either a rise in blood pressure or no definite change. Acute mechanical distention of aortic ring of the left ventricle invariably produces a fall in blood pressure even when both vagi are severed. Mechanical and electrical stimulation of the annulus of Vieussens after all vagal strands are severed invariably produces an increase in blood pressure.

**Cannell, D. E.: Congenital Aneurysm of the Interventricular Septum.** Am. J. Path. **6**: 477, 1930.

The clinical and pathological findings in two cases with congenital aneurysm of the interventricular septum are reported. The absence of clinical signs and symptoms in both cases wherein marked distortion of the normal anatomy was present is remarkable.

Photographs of the specimens are included.

A critical study of these cases adds further evidence in favor of these anomalies being congenital malformations rather than the terminal results of endocarditis.

**Burkhardt, E. A., Jr.: Marked Dilatation of the Left Auricle of the Heart.** Am. J. Path. 6: 463, 1930.

A man, aged twenty-three years, was admitted with a diagnosis of chronic cardiac rheumatic valvular disease with auricular fibrillation with embolism of the left internal capsule and probable subacute bacterial endocarditis. Death occurred the following day.

Autopsy showed, aside from the usual findings in the heart, a left auricle which was markedly dilated, the right border extending 8 cm. to the right of the mid-clavicular line in the region of the fourth rib. The left border lay in the arch of the aorta. The auricle had a capacity of 593 c.c. of fluid after fixation. The mitral valve was stenosed to a slit-like opening. There was a mural thrombus within the left auricle.

**Barnard, William G.: A Case of Paradoxical Embolism with Blood-Clot Lodged in Foramen Ovale.** Quart. J. Med. 23: 305, 1930.

The patient, a well-nourished and well-developed man of sixty-three years, was under treatment for carcinoma of the prostate. A suprapubic cystostomy was performed and radium inserted into the growth. Recovery was satisfactory, and the patient was getting up at the end of a fortnight. On the sixteenth day, he was kept in bed on account of symptoms ascribed to indigestion. In the evening of that day he died quite suddenly, while talking to another patient.

At the post-mortem examination, a mass of coiled, mixed, red, pink and grey laminated clot with a rippled surface was found completely filling the right and left pulmonary arteries and extending for a short distance into their main branches. An entirely separate clot of similar formation and about 15 cm. long was caught in the foramen ovale in such a way that its greater length hung free in the left auricle and down into the left ventricle, while a much shorter, thicker part projected into the right auricle. It seemed that the clot in the foramen ovale was of a similar sort to that in the pulmonary artery and not a part broken off.

Photograph of the specimen is included in the report.

**Cox, Ralph L.: Aneurysm of the Coronary Arteries.** Am. J. M. Sc. 180: 37, 1930.

A case of aneurysm of the right coronary artery is reported. There were no clinical findings suggesting this lesion. In addition to the coronary aneurysm and to nodular inequalities in the circumferences of the medium-sized arteries, there was a large saccular aneurysm of the abdominal aorta and a fusiform aneurysm of the right common iliac artery. There was an extreme degree of sclerosis of the coronary arteries with occlusion of the left ramus descendens and extensive myocardial infarction.

**Gilchrist, A. Rae, and Ritchie, W. T.: The Ventricular Complexes in Myocardial Infarction and Fibrosis.** Quart. J. Med. 23: 273, 1930.

A study of 148 cases of serial electrocardiograms indicates that sequential alterations of the R-T segment and of T, occurring in the course of a short period of time are strong presumptive evidence of myocardial infarction. Similar changes developing more slowly may be observed apart from myocardial infarction and may be due to dystrophic myocardial fibrosis following chronic progressive coronary sclerosis. The evidence available at the present time does not lend support to the view that the form of the electrocardiographic distortion can be regarded as a definite localizing sign of the infarct.

**Bach, Francis: On the Clinical Significance of Right Branch Bundle Block.** Quart. J. Med. 23: 261, 1930.

Eighty cases of branch bundle block have been investigated clinically and electrocardiographically. They have been divided into three groups determined by the etiology of the lesion, namely, cardiovascular-degenerative, syphilitic, and rheumatic. The author believes that the clinical picture and the prognosis is different and distinct in these three groups.

In group one, consisting of fifty patients, ten have died since being under observation, fifteen are at present untraced, and twenty-five alive. In group two, of seventeen syphilitic cases, nine are already dead, four are untraced, and four are alive. In group three, of eleven rheumatic cases with mitral stenosis, one has died, seven are still attending the hospital and three are untraced.

**Hyman, Albert S., and Parsonnet, Aaron E.: Bundle-Branch Block. The Phenomenon of Its Development in Relation to Axis Deviation of the Heart.** Arch. Int. Med. 45: 868, 1930.

In a group of 469 cases showing left axial deviation of the heart the authors have studied 46 that show an upright QRS and a negative T-wave in Lead I and a downward QRS and an upright T-wave in Lead III. These cases have been followed for periods ranging from eight months to four years. Of the forty-six patients, twenty-one developed true right bundle-branch block with no change of sinus rhythm, and eight developed auricular fibrillation with bundle-branch block; four showed complete auricular and ventricular dissociation with bundle-branch block, and the remaining thirteen showed right bundle-branch block with an extrasystolic arrhythmia from single and multiple foci.

In this connection, the authors were able to watch one case of right axis deviation of the heart which developed into a true left bundle-branch block prior to the death of the patient. Considerable prognostic information may thus be secured from close scrutiny of all electrocardiograms taken during age periods mentioned in the study.

The onset of bundle-branch block may sometimes be suspected many months and even years prior to the actual development of the typical delayed conduction phenomena which are so characteristic of this condition.

**Coombs, Carey F.: Observations on the Etiological Correspondence Between Anginal Pain and Cardiac Infarction.** Quart. J. Med. 23: 233, 1930.

The author has studied a group of 86 cases in which cardiac pain persistent in character and not necessarily excited by effort was followed by evidence of gross injury to the wall of the heart; also a second group of cases in which the pain was excited by effort, relieved by its cessation, and not followed by a structural sequelae. The age and sex incidence of the two groups correspond closely with one another.

The angina of effort occurs principally in association with cardiac syphilis, high arterial tension and senile degeneration of the heart. Cardiac infarction occurred in the second and third of these three etiological groups but rarely in the first. Both syndromes are rare in the other infective and toxic diseases of the heart.

The author concludes that pain of an anginal kind is produced by those types of diseases which fail to forward oxygenated blood to the cardiac muscle.

**Werley, G.: Coronary Infarct and Angina with Abdominal Symptoms.** M. J. & Rec. 131: 367, 1930.

The author believes that coronary infarction is similar in its etiology to infarction which may occur in other parts of the body with pronounced symptoms of

pain. This is particularly true of infarction in the abdominal arteries. He believes that sclerosis of the arteries is a strong predisposing factor in the production of coronary infarction. He describes four cases that showed mesentery thrombosis or symptoms referable to the abdomen which might be differentiated from coronary infarction and angina.

The author believes there is little or no relation of cause and effect between gallstones and coronary sclerosis. In a series of 575 autopsies, there were 26 instances of cardiac infarction none of which showed signs of abdominal disease. He believes there may be a common cause between gallstones and coronary sclerosis, since cholesterol is the main constituent of both gallstones and the atheromatous plaques of arteriosclerosis; therefore, in patients showing arteriosclerosis there might be found some evidence of gallstones and cholecystitis.

The author discusses the possibility of angina pectoris being due to an allergic disturbance within the heart muscle. He points out that similar disturbances can occur in the lungs, abdomen, and other parts of the body associated with vasomotor changes. He also reports three cases of coronary infarction in which there was marked hematemesis.

**Burton, J. A. G., Cowan, John, Kay, J. Hunter, Marshall, A. J., Rennie, J. K., Ramage, J. H., and Teacher, J. H.: Four Cases of Fibrosis of the Myocardium With Electrocardiographic and Post-Mortem Examinations.** Quart. J. Med. 23: 293, 1930.

Four cases of coronary artery disease are described with a history of cardiac ailment up to eight years. In the first case after the initial coronary occlusion with the usual symptoms, working capacity was maintained for seven years, then anginal attacks followed for six months, in one of which death occurred.

Electrocardiograms showed a type of T-wave inversion indicating infarction of the posterior ventricular wall. The inversion first observed thirty-seven days after the infarction had not disappeared six and one-half years later. The second, third, and fourth cases were similar in that there was a history of cardiac distress, edema, breathlessness, and gradual congestive failure resulting in death. In the second case the anterior coronary artery was almost occluded, and there was fibrosis in the muscle supplied. In the third case, the descending branch of the coronary artery was occluded, and there were patches of fibrosis in the ventricular wall. In the fourth case the descending branch of the left coronary artery was almost occluded, and the right coronary was markedly narrowed. There was dystrophic fibrosis in the left ventricular wall and part of the septum.

These cases were not associated with characteristic electrocardiographic changes.

**Davies, H. Whitridge, and Holmes, Geoffrey: Some Effects of Warm Immersion Baths Upon the Circulation.** Quart. J. Med. 23: 327, 1930.

Detailed findings of pulse rate, blood pressure, circulaton rates and metabolism on three normal human subjects in fifteen different experimental baths are recorded. The pulse rate was increased, the systolic blood pressure either increased slightly or was maintained, while the diastolic blood pressure was reduced sometimes to a considerable extent. The circulation rate showed, as a rule, a small increase but was markedly reduced in two instances when considerable pulmonary hyperventilation and consequent gaseous alkalosis occurred.

**Bohrod, Milton G.: Rheumatic Pericarditis With Polypoid Formations.** Arch. Path. 10: 51, 1930.

In the pericardium of a man twenty-seven years old with typical rheumatic heart disease, a peculiar polypoid mass was found. Clinical evidence of pericarditis had

never been observed. Necropsy disclosed an old mitral and aortic valvulitis with a recent endocarditis engrafted on this process. All the chambers were dilated, and hypertrophy occurred in the muscle. The heart with the pericardium weighed 1400 grams.

The unusual features were in the pericardium. There were adhesions between the pericardial layers in most places, fibrinous and easily broken, but in the region of the interventricular septum anteriorly the two layers were firmly bound together. About 75 or 100 c.c. of cloudy, slightly brownish fluid were found in the sac. Both layers were covered by shaggy fibrinous material easily stripped off. The color of the pericardium was chocolate brown.

At the reflection of the parietal pericardium from the right auricle posteriorly hung a large hydatidiform mass. The distal two-thirds of this mass were made up of several dozen bluish polypoid bodies from 4 to 15 mm. in diameter, a few of them solid but most of them filled with blood in various stages of inspissation. In some, the contents were thick and chocolate brown. From the posterior part of the mass hung a long loop of firm tissue 1.5 mm. thick. Over the surface of the auricle and underneath the auricular appendage there were tiny brownish projections from 0.5 to 3 mm. in length usually solid but occasionally cystic, the contents of the cysts being old blood.

Microscopically, the polypoid bodies were cysts with walls of varying thickness, lined by a single layer of flattened cells and filled with erythrocytes.

Detailed description of the specimen follows.

**Perry, C. B.: The Main Branches of the Coronary Arteries in Acute Rheumatic Carditis.** Quart. J. Med. **23**: 241, 1930.

This investigation was incited by the discovery of severe intimal thickening in the main branches of the coronary arteries, considerably reducing their lumen, in a child with severe rheumatic carditis who during life suffered from typical anginal pain. In order to see whether these changes were exceptional or usual in this disease, blocks, which included the main coronary arteries, were taken from the next eight fatal cases of rheumatic carditis that were submitted to autopsy. All of these hearts showed changes in one or more of the main branches of the coronary artery which though less intense than those in the first case were essentially similar in nature. The lesion is a general panarteritis consisting of: (a) intimal thickening more or less cellular; (b) degenerative and inflammatory lesions of the media; (c) inflammatory infiltration and fibrosis of the adventitia.

**Hill, N. Gray, and Allan, Mary: The Family Incidence of Juvenile Rheumatism.** Brit. M. J. p. 949, May 24, 1930.

Information has been collected from the parents of 400 rheumatic children relating to the incidence of rheumatic manifestations in their families. Of the 400 families investigated, the total number of children was 2,156 and the total number of rheumatic children in these families was 540.

The present rather limited inquiry seems to indicate that very few of the brothers and sisters of the rheumatic patients developed the disease. The possibility is suggested that with more exhaustive inquiry made only after the entire family have passed the age of twenty-five years, an increased number of rheumatic members might be found.

In the series, there were eight pairs of twins and in not a single incidence have both twins developed recognizable manifestations of rheumatism. In only six families do both father and mother give a history of juvenile rheumatism, and in only a comparatively small number of incidences is there a history of rheumatism among both the father's and the mother's relatives.

**Ernstene, A. Carlton: Erythrocyte Sedimentation. Plasma Fibrinogen and Leukocytosis as Indices of Rheumatic Infection.** Am. J. M. Sc. **180:** 12, 1930.

The corrected sedimentation index, plasma fibrinogen content and leucocyte count were measured at frequent intervals in 22 patients with rheumatic fever. At the height of the illness the corrected sedimentation index showed a greater relative increase above normal than did the leucocyte count. Both the leucocyte count and the index were depressed somewhat by salicylates, but in general the sedimentation index seemed to be less affected than the white blood cell count. A slight increase in the leucocyte count and corrected sedimentation index followed by a prompt return to the previous level was observed frequently after discontinuance of salicylates.

With exacerbations of the infection in the polycyclic and continuous types of the disease, there was usually a greater relative increase in the corrected sedimentation index than in the leucocyte count. In all types of the disease, the index, with few exceptions, remained elevated for several days to a few weeks after the leucocyte count had become normal.

The author concludes that the corrected sedimentation index is a test preferable to estimations of the plasma fibrinogen content on account of its greater simplicity. He also believes that the rheumatic infection cannot be considered arrested until the corrected sedimentation index has become and remains normal.

**Faulkner, James M.: The Significance of Sinus Arrhythmia in Old People.** Am. J. M. Sc. **180:** 42, 1930.

The pathological significance of sinus arrhythmia in old people with organic heart disease is discussed. Case reports from four patients are presented. Analyses of hospital records show that sinus arrhythmia in patients over fifty years of age is more frequently associated with evidence of organic heart disease than is normal rhythm. Support is lent to the observation that sinus arrhythmia may at times represent a reflex response to abnormal efferent stimuli from a diseased heart or aorta.

**Riseman, Joseph E. F., and Weiss, Soma: The Symptomatology of Arterial Hypertension.** Am. J. M. Sc. **180:** 47, 1930.

An analysis of the complaints of 1,090 ambulatory patients with primary (essential) hypertension indicates that the following symptoms are present in more than 20 per cent of the cases: headache in 43.3 per cent, dizziness in 40.3 per cent, aches and pains in 38.7 per cent, dyspnea in 27.7 per cent, nycturia in 25.9 per cent.

Arterial hypertension is not associated with characteristic symptomatology. Almost all the symptoms of patients with arterial hypertension are referable to a disturbance of the central nervous system and are expressions of a disordered vasomotor system.

Among conditions with normal blood pressure, menopause, obesity, and psychoneurosis showed symptoms similar to those of arterial hypertension. All four conditions frequently exhibit vasomotor instability.

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